

1/2

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NEWS 13 DEC 14 GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 14 DEC 18 CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 15 DEC 18 CA/CAplus patent kind codes updated
NEWS 16 DEC 18 MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 17 DEC 18 MEDLINE updated in preparation for 2007 reload
NEWS 18 DEC 27 CA/CAplus enhanced with more pre-1907 records
NEWS 19 JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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10 / 715,773

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DICTIONARY FILE UPDATES: 10 JAN 2007 HIGHEST RN 917201-58-2

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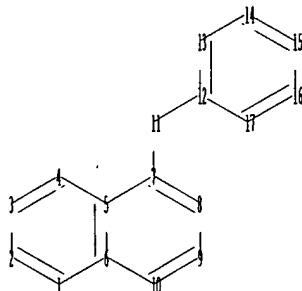
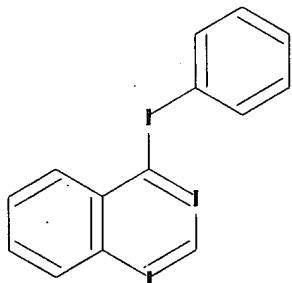
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<http://www.cas.org/ONLINE/UG/reqprops.html>

=>
Uploading C:\Program Files\Stnexp\Queries\10715773.str



chain nodes :

11

ring nodes :

1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17

chain bonds :

7-11 11-12

ring bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-17 13-14 14-15
 15-16 16-17

15-16 16-
exact/norm

exact, non-
7-11 11-12

normalized bonds :

normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-17 13-14 14-15
 15-16 16-17

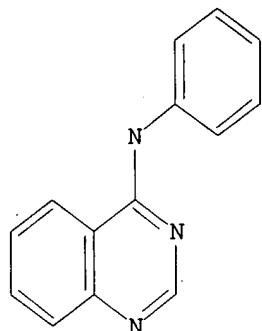
10/ 715,773

isolated ring systems :
containing 1 : 12 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom

L1 STRUCTURE UPLOADED

=> d L1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11 sample
SAMPLE SEARCH INITIATED 09:44:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1397 TO ITERATE

100.0% PROCESSED 1397 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 25698 TO 30182
PROJECTED ANSWERS: 14435 TO 17843

L2 50 SEA SSS SAM L1

=> s 11 ful
FULL SEARCH INITIATED 09:44:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 29158 TO ITERATE

100.0% PROCESSED 29158 ITERATIONS 16567 ANSWERS
SEARCH TIME: 00.00.01

L3 16567 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION

10/ 715,773

FULL ESTIMATED COST 172.10 172.31

FILE 'HCAPLUS' ENTERED AT 09:44:24 ON 11 JAN 2007
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FILE COVERS 1907 - 11 Jan 2007 VOL 146 ISS 3
FILE LAST UPDATED: 10 Jan 2007 (20070110/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 13
L4      2367 L3

=> s 14 not methylenedioxy
     8517 METHYLENEDIOXY
L5      2358 L4 NOT METHYLENEDIOXY

=> s 15 not py>1999
     7577142 PY>1999
L6      319 L5 NOT PY>1999
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=> d his

(FILE 'HOME' ENTERED AT 09:43:33 ON 11 JAN 2007)

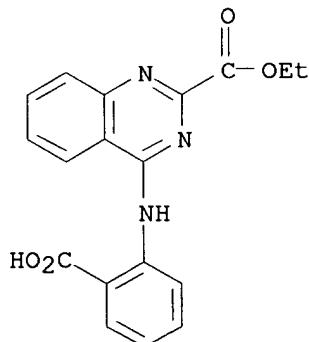
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FILE 'REGISTRY' ENTERED AT 09:43:47 ON 11 JAN 2007
L1      STRUCTURE UPLOADED
L2      50 S L1 SAMPLE
L3      16567 S L1 FUL

FILE 'HCAPLUS' ENTERED AT 09:44:24 ON 11 JAN 2007
L4      2367 S L3
L5      2358 S L4 NOT METHYLENEDIOXY
L6      319 S L5 NOT PY>1999
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=> d 16 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 319 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:675531 HCAPLUS
DOCUMENT NUMBER: 133:362749
TITLE: Synthesis and antiinflammatory activity of ethyl 4-(anilino substituted)-2-quinazolinecarboxylates
AUTHOR(S): Mekuskiene, Giedrute; Udrenaite, Emilia; Gaidelis, Povilas; Vainilavicius, Povilas

CORPORATE SOURCE: Faculty of Chemistry, Vilnius University, Vilnius,
LT-2006, Lithuania
 SOURCE: Chemija (1999), 10(3), 214-217
 CODEN: CHMIES; ISSN: 0235-7216
 PUBLISHER: Academia
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 133:362749
 AB Treatment of Et 4-oxo-3,4-dihydro-2-quinazolinecarboxylate with thionyl chloride resulted in Et 4-chloro-3,4-dihydro-2-quinazolinecarboxylate formation. The latter reacted with aromatic amines in acidified water or benzene to form Et 4-(anilino substituted)-2-quinazolinecarboxylate possessing antiinflammatory activity.
 IT 202746-97-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and antiinflammatory activity of Et anilinoquinazolinecarboxylates)
 RN 202746-97-2 HCPLUS
 CN 2-Quinazolinecarboxylic acid, 4-[(2-carboxyphenyl)amino]-, 2-ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:228537 HCPLUS
 DOCUMENT NUMBER: 132:342816
 TITLE: Structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents
 AUTHOR(S): Ghosh, Sutapa; Narla, Rama Krishna; Zheng, Yaguo; Liu, Xing-Ping; Jun, Xiao; Mao, Chen; Sudbeck, Elise A.; Uckun, Fatih M.
 CORPORATE SOURCE: Parker Hughes Cancer Center, Departments of Structural Biology, Parker Hughes Institute, St Paul, MN, 55113, USA
 SOURCE: Anti-Cancer Drug Design (1999), 14(5), 403-410
 CODEN: ACDDEA; ISSN: 0266-9536
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In a systematic effort to design inhibitors of the epidermal growth factor receptor (EGFR) family protein tyrosine kinases (PTK) as anti-cancer agents, we have constructed a three-dimensional homol. model of the EGFR kinase domain and used mol. modeling methods for the structure-based

design of analogs of the active metabolite of leflunomide (LFM) with potent and specific inhibitory activity against EGFR. These docking studies identified α -cyano- β -hydroxy- β -methyl-N-[4-(trifluoromethoxy)phenyl]-p ropanamide (LFM-A12) as our lead compound, which was predicted to bind to the EGFR catalytic site in a planar conformation. LFM-A12 inhibited the proliferation ($IC_{50} = 26.3 \mu M$) and in vitro invasiveness ($IC_{50}=28.4 \mu M$) of EGFR pos. human breast cancer cells in a concentration-dependent fashion. Similarly, the model of the EGFR binding pocket

was used in combination with docking procedures to predict the favorable placement of chemical groups with defined sizes at multiple modification sites on another class of EGFR inhibitors, the 4-anilinoquinazoline. This approach has led to the successful design of a dibromo quinazoline derivative, WHI-P97, which had an estimated K_i value of $0.09 \mu M$ from modeling studies and a measured IC_{50} value of $2.5 \mu M$ in EGFR kinase inhibition assays. WHI-P97 effectively inhibited the in vitro invasiveness of EGFR-pos. human cancer cells in a concentration-dependent manner. However, unlike LFM-A12, the quinazoline compds. are not specific for EGFR.

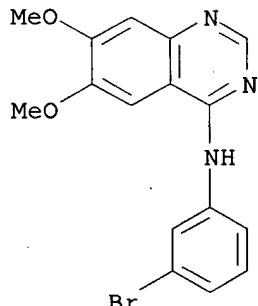
IT 153436-54-5, WHI-P 79

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents)

RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:73533 HCPLUS

DOCUMENT NUMBER: 132:247362

TITLE: Induction of DNA replication by peroxisome proliferators is independent of both tumor necrosis factor α priming and EGF-receptor tyrosine kinase activity

AUTHOR(S): Chevalier, Stephan; Macdonald, Neil; Roberts, Ruth A.

CORPORATE SOURCE: AstraZeneca, Central Toxicology Laboratory Cancer Biology Group, Cheshire, SK10 4TJ, UK

SOURCE: Journal of Cell Science (1999), 112(24), 4785-4791

CODEN: JNCSAI; ISSN: 0021-9533

PUBLISHER: Company of Biologists Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators (PPs) cause hepatocyte proliferation and tumorigenesis in rodent liver. PPs induce hepatocyte DNA synthesis

although the mechanism is unclear. Tumor necrosis factor α (TNF α) and epidermal growth factor (EGF) have been implicated in mediating this growth response since these factors induce a threefold and 17.2-fold increase, resp., in DNA synthesis in rat primary hepatocyte cultures. Previously, others have suggested that TNF α acts as a primer to sensitize hepatocytes to the proliferative effects of growth factors. Indeed, here the authors show that costimulation with TNF α and a suboptimal (4-20% of optimal) concentration of EGF permits an 11.7-fold increase in DNA synthesis in rat primary hepatocyte cultures. The PP nafenopin induced a 2.3-fold increase in DNA synthesis but there was no further increase upon co-administration of either TNF α or a suboptimal concentration of EGF. Furthermore, there was no gross disregulation of the CDK and cyclin protein expression profile upon stimulation with nafenopin. Using a specific epidermal growth factor receptor tyrosine kinase inhibitor (4-(3-chloro-4-fluorophenylamino)-7-methoxy-6-(3-[1-pyrrolidino])-propoxyquinazoline, EGFR-TKI), the authors show that signalling through EGF-R is not required for nafenopin-induced DNA synthesis. The EGFR-TKI also prevented progression into S phase upon stimulation with TNF α , but DNA synthesis was not reduced to control levels, indicating that TNF α has a mitogenic activity in the absence of EGF signalling. Therefore, although TNF α can act as a priming factor for growth factors such as EGF, nafenopin does not appear to act via this mechanism.

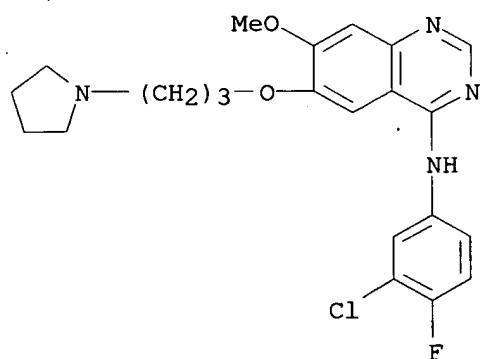
IT 184475-45-4

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(EGF-receptor tyrosine kinase inhibitor; DNA replication induction by peroxisome proliferators is independent of both tumor necrosis factor α priming and EGF-receptor tyrosine kinase activity)

RN 184475-45-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(1-pyrrolidinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:54949 HCPLUS

DOCUMENT NUMBER: 132:329420

TITLE: Specificity of α -cyano- β -hydroxy- β -methyl-N-[4-(trifluoromethoxy)phenyl]-p ropanamide as an inhibitor of the epidermal growth factor receptor tyrosine kinase

AUTHOR(S): Ghosh, Sutapa; Zheng, Yaguo; Jun, Xiao; Mahajan,

CORPORATE SOURCE: Sandeep; Mao, Chen; Sudbeck, Elise A.; Uckun, Fatih M.
Parker Hughes Cancer Center, Departments of Structural
Biology, Hughes Institute, St.Paul, MN, 55113, USA

SOURCE: Clinical Cancer Research (1999), 5(12), 4264-4272
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The epidermal growth factor receptor (EGFR) tyrosine kinase has an essential function for the survival of human breast cancer cells. In a systematic effort to design potent and specific inhibitors of this receptor family protein tyrosine kinase (PTK) as antibreast cancer agents, we recently reported the construction of a three-dimensional homol. model of the EGFR kinase domain. In this model, the catalytic site is defined by two β -sheets that form an interface at the cleft between the NH₂-terminal and COOH-terminal lobes of the kinase domain. Our modeling studies revealed a distinct, remarkably planar triangular binding pocket within the kinase domain with approx. dimensions of 15 Å + 12Å + 12Å, and the thickness of the binding pocket is .apprx.7Å with an estimated volume of .apprx.600 Å³ available for inhibitor binding. Mol. docking studies had identified α -cyano- β -hydroxy- β -methyl-N-[4-(trifluoromethoxy)phenyl]-p ropanamide (LFM-A12) as our lead inhibitor, with an estimated binding constant

of 13 μ M, which subsequently inhibited EGFR kinase in vitro with an IC₅₀ value of 1.7 μ M. LFM-A12 was also discovered to be a highly specific inhibitor of the EGFR. Even at very high concns. ranging from 175-350 μ M, this inhibitor did not affect the enzymic activity of other PTKs, including the Janus kinases JAK1 and JAK3, the Src family kinase HCK, the Tec family member Bruton's tyrosine kinase, SYK kinase, and the receptor family PTK insulin receptor kinase. This observation is in contrast to the activity of a quinazoline inhibitor tested as a control, 4-(3-bromo, 4-hydroxyanilino)-6,7-dimethoxyquinazoline, which was shown to inhibit EGFR and other tyrosine kinases such as HCK, JAK3, and SYK.

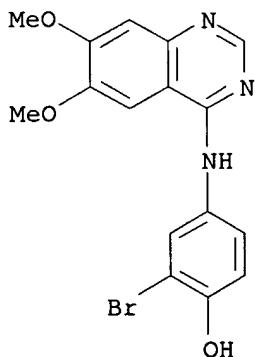
IT 211555-04-3, WHI-P154

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epidermal growth factor receptor tyrosine kinase inhibitor LFM-A12)

RN 211555-04-3 HCPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

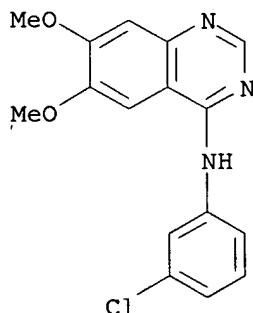


REFERENCE COUNT:

40

THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:22595 HCAPLUS
 DOCUMENT NUMBER: 132:288733
 TITLE: Growth inhibition of psoriatic keratinocytes by quinazoline tyrosine kinase inhibitors
 AUTHOR(S): Powell, T. J.; Ben-Bassat, H.; Klein, B. Y.; Chen, H.; Shenoy, N.; McCollough, J.; Narog, B.; Gazit, A.; Harzstark, Z.; Chaouat, M.; Levitzki, R.; Tang, C.; McMahon, J.; Shawver, L.; Levitzki, A.
 CORPORATE SOURCE: SUGEN, Inc., Redwood City, CA, 94063, USA
 SOURCE: British Journal of Dermatology (1999), 141(5), 802-810
 CODEN: BJDEAZ; ISSN: 0007-0963
 PUBLISHER: Blackwell Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Psoriasis is characterized by hyperproliferation of keratinocytes associated with an inflammatory infiltrate in the epidermis. Among factors which may be related to hyperplasia of psoriatic keratinocytes is the persistent autocrine stimulation of the epidermal growth factor receptor (EGFR) by transforming growth factor- α . Owing to the pivotal role of the EGFR in driving the growth of human psoriatic keratinocytes, we examined two selective inhibitors of EGFR kinase activity: 4-(3-bromophenylamino)-6,7-dimethoxyquinazoline (AG1517/SU5271) and 4-(3-chlorophenylamino)-6,7-dimethoxyquinazoline (AG1478) on psoriatic keratinocytes. SU5271 potently inhibits ligand-induced autophosphorylation of EGFR, and downstream signal transduction events, including DNA replication and cell cycle progression. SU5271, at micromolar concns., inhibited the proliferation of keratinocytes isolated from psoriatic lesions in excellent correlation with its EGFR kinase inhibitory activity in these cells. Biol. active concns. of SU5271 penetrated human cadaver skin, suggesting that this compound is a strong candidate as an antipsoriatic agent.
 IT 153436-53-4, AG1478
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (growth inhibition of psoriatic keratinocytes by quinazoline tyrosine kinase inhibitors via inhibition of EGF signaling)
 RN 153436-53-4 HCAPLUS
 CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 132:160709
 TITLE: Antiangiogenic agents
 AUTHOR(S): Klohs, Wayne D.; Hamby, James M.
 CORPORATE SOURCE: Department of Drug Development, Parke-Davis
 Pharmaceutical Research, Warner-Lambert Company, Ann Arbor, MI, 48105, USA
 SOURCE: Current Opinion in Biotechnology (1999), 10(6), 544-549
 CODEN: CUOB3; ISSN: 0958-1669
 PUBLISHER: Current Biology Publications
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 32 refs. A greater understanding of the complex process of tumor-induced angiogenesis, coupled with the notion that tumors require a blood supply to both grow and metastasize, has fueled the search for agents that block or disrupt the angiogenic process. Because normal vascular endothelial cells (ECs) turn over so slowly, conventional wisdom suggests that an antiangiogenic approach to cancer therapy should offer improved efficacy and reduced toxicity, without the potential for drug resistance. Numerous report have identified small mols. or antibodies that can interfere with one or more key steps in EC signaling, migration or differentiation. Three new compds., ZD4190, SU6668 and PD 0173074, have been reported during the past year to have significant and selective antiangiogenic activity, as well as antitumor activity.

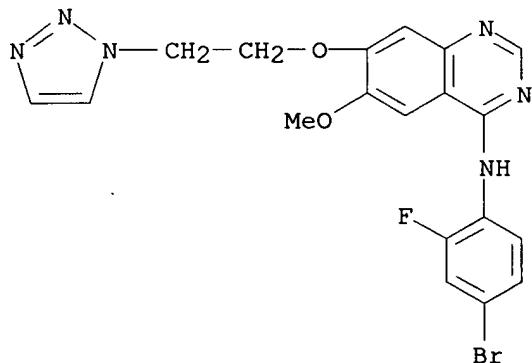
IT 257938-36-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiangiogenic agents for treatment of cancer)

RN 257938-36-6 HCPLUS

CN 4-Quinazolinamine, N-(4-bromo-2-fluorophenyl)-6-methoxy-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:784580 HCPLUS

DOCUMENT NUMBER: 132:151769

TITLE: Design and Structure-Activity Relationship of a New Class of Potent VEGF Receptor Tyrosine Kinase

Inhibitors

AUTHOR(S): Hennequin, Laurent F.; Thomas, Andrew P.; Johnstone, Craig; Stokes, Elaine S. E.; Ple, Patrick A.; Lohmann, Jean-Jacques M.; Ogilvie, Donald J.; Dukes, Mike; Wedge, Steve R.; Curwen, Jon O.; Kendrew, Jane; Lambert-van der Brempt, Christine

CORPORATE SOURCE: AstraZeneca Zeneca Pharma Centre de Recherches Z.I. La Pompeille, Reims, 51689, Fr.

SOURCE: Journal of Medicinal Chemistry (1999), 42(26), 5369-5389

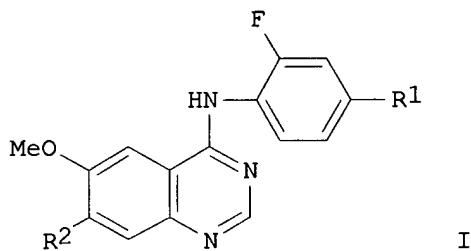
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB A series of substituted 4-anilinoquinazolines and related compds. were synthesized as potential inhibitors of vascular endothelial growth factor (VEGF) receptor (Flt and KDR) tyrosine kinase activity. Enzyme screening indicated that a narrow structure-activity relationship (SAR) existed for the bicyclic ring system, with quinazolines, quinolines, and cinnolines having activity and with quinazolines and quinolines generally being preferred. Substitution of the aniline was investigated and clearly indicated that small lipophilic substituents such as halogens or Me were preferred at the C-4' position. Small substituents such as hydrogen and fluorine are preferred at the C-2' position. Introduction of a hydroxyl group at the meta position of the aniline produced the most potent inhibitors of Flt and KDR tyrosine kinases activity with IC₅₀ values in the nanomolar range. Investigation of the quinazoline C-6 and C-7 positions indicates that a large range of substituents are tolerated at C-7, whereas variation at the C-6 is more restricted. At C-7, neutral, basic, and heteroarom. side chains led to very potent compds., as illustrated by the methoxyethoxy derivative I [R1 = 4-Cl, R2 = OCH₂CH₂OMe] (IC₅₀ < 2 nM). These inhibitors proved to be very selective inhibitors of Flt and KDR tyrosine kinase activity when compared to that associated with the FGF receptor (50- to 3800-fold). Observed enzyme profiles translated well with respect to potency and selectivity for inhibition of growth factor stimulated proliferation of human umbilical vein endothelial cells (HUVECs). Oral administration of selected compds. to mice produced total plasma levels 6 h after dosing of between 3 and 49 μM. In vivo efficacy was demonstrated in a rat uterine edema assay where significant activity was achieved at 60 mg/kg with I [R1 = Me, R2 = OMe]. Inhibition of growth of human tumors in athymic mice has also been demonstrated: I [R1 = Br, R2 = 2-(1,2,3-triazol-1-yl)ethoxy] inhibited the growth of established Calu-6 lung carcinoma xenograft by 75% (P < 0.001, one tailed t-test) following daily oral administration of 100 mg/kg for 21 days.

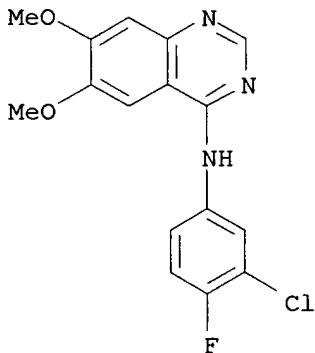
IT 153437-03-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and structure-activity relationship of arylaminoquinazoline VEGF receptor tyrosine kinase inhibitors)

RN 153437-03-7 HCPLUS

CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-6,7-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:782032 HCPLUS

Correction of: 1996:73866

DOCUMENT NUMBER: 131:351298

Correction of: 124:232395

TITLE:

Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor

AUTHOR(S):

Rewcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.

CORPORATE SOURCE:

School of Medicine, University of Auckland, Auckland, 92019, N. Z.

SOURCE:

Journal of Medicinal Chemistry (1996), 39(4), 918-928
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

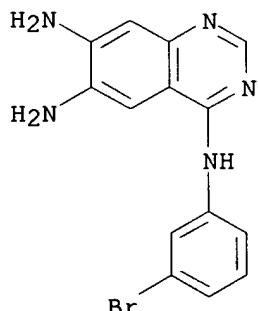
AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC_{50} 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC_{50} of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C- γ 1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most

potent compds. were linear pyrazoloquinazoline analogs (IC₅₀ 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC₅₀ 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC₅₀ of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC₅₀s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC₅₀ 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC₅₀ of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC₅₀ 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very

selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC₅₀ 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC₅₀ of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC₅₀s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

IT 169205-87-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)

RN 169205-87-2 HCPLUS
 CN 4,6,7-Quinazolinetriamine, N4-(3-bromophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 9 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:777760 HCPLUS
 DOCUMENT NUMBER: 132:87758
 TITLE: Tyrosine Kinase Inhibitors. 16. 6,5,6-Tricyclic Benzothieno[3,2-d]pyrimidines and Pyrimido[5,4-b]- and -[4,5-b]indoles as Potent Inhibitors of the Epidermal Growth Factor Receptor Tyrosine Kinase
 AUTHOR(S): Showalter, H. D. Hollis; Bridges, Alexander J.; Zhou, Hairong; Sercel, Anthony D.; McMichael, Amy; Fry, David W.
 CORPORATE SOURCE: Departments of Chemistry and Cancer Research, Parke-Davis Pharmaceutical Research Division of

SOURCE: Warner-Lambert Company, Ann Arbor, MI, 48105, USA
 Journal of Medicinal Chemistry (1999), 42(26),
 5464-5474

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several elaborations of the fundamental anilinopyrimidine pharmacophore have been reported as potent and selective inhibitors of the epidermal growth factor receptor (EGFr) tyrosine kinase. This paper reports on a series of inhibitors whereby some 6,5-bicyclic heteroarom. systems were fused through their C-2 and C-3 positions to this anilinopyrimidine pharmacophore. Although the resulting tricycles did not produce the enormous potency of some of the (5/6),6,6-bicyclic systems, the best of them had IC50s for the EGFr TK around 1 nM. Investigation of 4-position side chains in the indolopyrimidines confirmed that m-bromoaniline was an optimal substituent for potency. Investigation of substitution within the C-(benzo)ring of benzothienopyrimidines confirmed that introduction of an extra ring can change sharply the effects of substituents when compared to similar bicyclic nuclei, and only two substituents were found which even moderately enhanced inhibitory activity over the parent compound for this series.

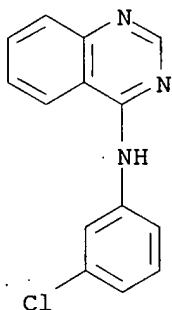
IT 88404-44-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(synthesis of benzothieno-, pyrimido- and indolo-pyrimidines as inhibitors of epidermal growth factor receptor tyrosine kinase)

RN 88404-44-8 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:735904 HCPLUS

DOCUMENT NUMBER: 132:44704

TITLE: Effects of changrolin on potassium currents in guinea pig and rabbit single heart cells

AUTHOR(S): Lu, Ling-Ling

CORPORATE SOURCE: Department of Physiology, College of Medicine, Xiamen University, Xiamen, 361005, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1999), 20(11), 1015-1018

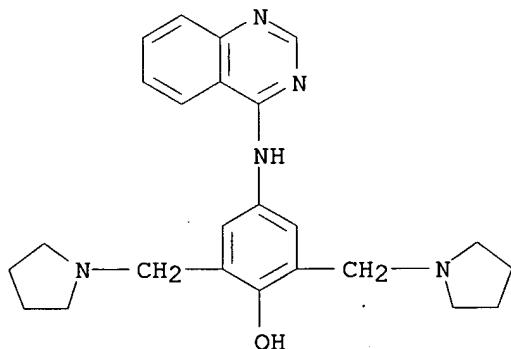
CODEN: CYLPDN; ISSN: 0253-9756

PUBLISHER: Kexue Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: English

- AB To elucidate whether or not changrolin (CRL), an antiarrhythmic drug, modifies the potassium currents in myocardial cells, a tight seal whole cell patch-clamp technique was used to record ITO, IK, and IK1 in single cells isolated from guinea pig and rabbit hearts. At a clin. relevant concentration, CRL 50 $\mu\text{mol}\cdot\text{L}^{-1}$ inhibited the transient outward current (ITO) by 17.7% \pm 2.4% (n = 8) in rabbit atrial cells. The voltage-dependence of steady-state inactivation of ITO was not affected by CRL. This concentration of CRL did not influence the time-independent inward rectifier or the delayed rectifier K⁺ currents (IK1 and IK, resp.) in rabbit and guinea pig ventricular cells. Thus, CRL inhibited ITO, but not IK nor IK1.
- IT 72063-47-9, Changrolin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of antiarrhythmic changrolin on potassium currents in guinea pig and rabbit single heart cells)
- RN 72063-47-9 HCPLUS
- CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

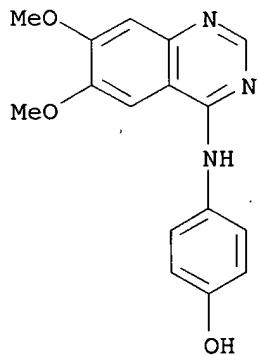


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L6 ANSWER 11 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:735691 HCPLUS
 DOCUMENT NUMBER: 132:202585
 TITLE: In vivo toxicity and pharmacokinetic features of the Janus kinase 3 inhibitor WHI-P131 [4-(4'hydroxyphenyl)-amino-6,7-dimethoxyquinazoline]
 AUTHOR(S): Uckun, Fatih M.; Ek, Onur; Liu, Xin-Ping; Chen, Chun-Lin
 CORPORATE SOURCE: Parker Hughes Cancer Center, Departments of Oncology, Immunology, Drug Discovery Program, Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Clinical Cancer Research (1999), 5(10), 2954-2962
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB 4-(4'Hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) is a potent and selective inhibitor of the Janus kinase 3, which triggers apoptosis in human acute lymphoblastic leukemia (ALL) cells. In this preclin. study, we evaluated the pharmacokinetics and toxicity of WHI-P131 in rats, mice, and cynomolgus monkeys. Following i.v. administration, the terminal elimination half-life of WHI-P131 was 73.2 min in rats, 103.4 min in mice,

and 45.0 min in monkeys. The i.v. administered WHI-P131 showed a very wide tissue distribution in mice. Following i.p. administration, WHI-P131 was rapidly absorbed in both rats and mice, and the time to reach the maximum plasma concentration (tmax) was 24.8 min in rats and 10.0 min in mice. Subsequently, WHI-P131 was eliminated with a terminal elimination half-life of 51.8 min in rats and 123.6 min in mice. The estimated i.p. bioavailability was 95% for rats, as well as for mice. WHI-P131 was quickly absorbed after oral administration in mice with a tmax of 5.8 min, but its oral bioavailability was relatively low (29.6%). The elimination half-life of WHI-P131 after oral administration was 297.6 min. WHI-P131 was not acutely toxic to mice at single i.p. bolus doses ranging from 0.5-250 mg/kg. Two cynomolgus monkeys treated with 20 mg/kg WHI-P131 and one cynomolgus monkey treated with 100 mg/kg WHI-P131 experienced no side effects. Plasma samples from WHI-P131-treated monkeys exhibited potent antileukemic activity against human ALL cells in vitro. To our knowledge, this is the first preclin. toxicity and pharmacokinetic study of a Janus kinase 3 inhibitor. Further development of WHI-P131 may provide the basis for new and effective treatment programs for relapsed ALL in clin. settings.

IT 202475-60-3, WHI-P131
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (in vivo toxicity and pharmacokinetic features of the Janus kinase 3 inhibitor WHI-P131)
 RN 202475-60-3 HCAPLUS
 CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:714280 HCAPLUS
 DOCUMENT NUMBER: 132:30431
 TITLE: Inhibition of epidermal growth factor receptor-associated tyrosine phosphorylation in human carcinomas with CP-358,774: dynamics of receptor inhibition *in situ* and antitumor effects in athymic mice
 AUTHOR(S): Pollack, Vincent A.; Savage, Douglas M.; Baker, Deborah A.; Tsaparikos, Konstantinos E.; Sloan, Donald E.; Moyer, James D.; Barbacci, Elsa G.; Pustilnik, Leslie R.; Smolarek, Teresa A.; Davis, John A.; Vaidya, Madhur P.; Arnold, Lee D.; Doty, John L.;

CORPORATE SOURCE: Iwata, Kenneth K.; Morin, Michael J.
 Department of Genomics, Targets and Cancer Research,
 Pfizer Central Research, Groton, CT, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics
 (1999), 291(2), 739-748

PUBLISHER: American Society for Pharmacology and Experimental
 Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phosphorylation of tyrosine residues on the epidermal growth factor (EGF) receptor (EGFr) is an important early event in signal transduction, leading to cell replication for major human carcinomas. CP-358,774 is a potent and selective inhibitor of the EGFr tyrosine kinase and produces selective inhibition of EGF-mediated tumor cell mitogenesis. To assess the pharmacodynamic aspects of EGFr inhibition, we devised an ex vivo ELISA for quantification of EGFr-specific tyrosine phosphorylation in human tumor tissue specimens obtained from xenografts growing s.c. in athymic mice. When coupled with pharmacokinetic analyses, this measurement can be used to describe the extent and duration of kinase inhibition in vivo. CP-358,774 is an effective, orally active inhibitor of EGFr-specific tyrosine phosphorylation (ED₅₀ = 10 mg/kg, single dose). It has a significant duration of action, producing, on average, a 70% reduction in

EGFr-associated phosphotyrosine over a 24-h period after a single 100 mg/kg dose. Inhibition of EGFr phosphotyrosine in an ex vivo assay format effectively ests. the potency and degree of inhibition of EGFr-dependent human L1CR-LON-HN5 head and neck carcinoma tumor growth. Substantial growth inhibition of human tumor xenografts was achieved with p.o. doses of the compound (ED₅₀ = 10 mg/kg q.d. for 20 days). Combination chemotherapy with cisplatin produced a significant response above that of cisplatin alone with no detectable effects on body weight or lethal toxicity. Taken together, these observations suggest that CP-358,774 may be useful for the treatment of EGFr-driven human carcinomas.

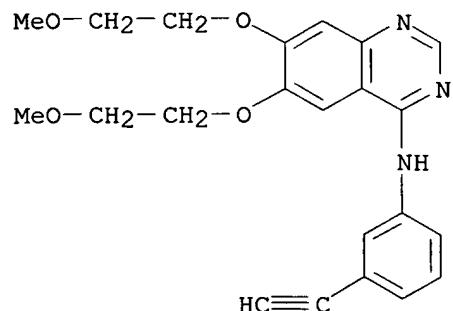
IT 183319-69-9, CP 358774

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of epidermal growth factor receptor-associated tyrosine phosphorylation in human carcinomas with antitumor CP-358,774 in mice)

RN 183319-69-9 HCPLUS

CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

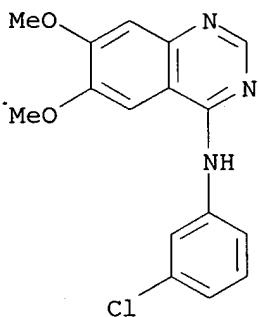


REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:714089 HCPLUS
DOCUMENT NUMBER: 132:31914
TITLE: Asbestos-induced phosphorylation of epidermal growth factor receptor is linked to c-fos and apoptosis
AUTHOR(S): Zanella, Christine L.; Timblin, Cynthia R.; Cummins, Andrew; Jung, Michael; Goldberg, Jonathan; Raabe, Rachel; Tritton, Thomas R.; Mossman, Brooke T.
CORPORATE SOURCE: Department of Pathology, University of Vermont College of Medicine, Burlington, VT, 05405, USA
SOURCE: American Journal of Physiology (1999), 277(4, Pt. 1), L684-L693
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

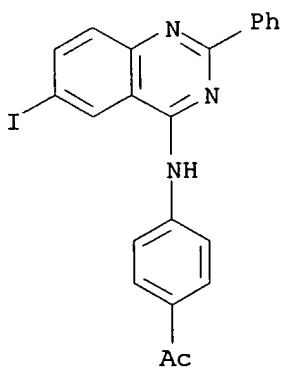
AB The authors examined the mechanisms of interaction of crocidolite asbestos fibers with the epidermal growth factor (EGF) receptor (EGFR) and the role of the EGFR-extracellular signal-regulated kinase (ERK) signaling pathway in early-response protooncogene (c-fos/c-jun) expression and apoptosis induced by asbestos in rat pleural mesothelial (RPM) cells. Asbestos fibers, but not the nonfibrous analog riebeckite, abolished binding of EGF to the EGFR. This was not due to a direct interaction of fibers with ligand, inasmuch as binding studies using fibers and EGF in the absence of membranes showed that EGF did not adsorb to the surface of asbestos fibers. Exposure of RPM cells to asbestos caused a greater than 2-fold increase in steady-state message and protein levels of EGFR ($P < 0.05$). The tyrphostin AG-1478, which inhibits the tyrosine kinase activity of the EGFR, but not the tyrphostin A-10, which does not affect EGFR activity, significantly ameliorated asbestos-induced increases in mRNA levels of c-fos but not of c-jun. Pretreatment of RPM cells with AG-1478 significantly reduced apoptosis in cells exposed to asbestos. The findings suggest that asbestos-induced binding to EGFR initiates signaling pathways responsible for increased expression of the protooncogene c-fos and the development of apoptosis. The ability to block asbestos-induced elevations in c-fos mRNA levels and apoptosis by small-mol. inhibitors of EGFR phosphorylation may have therapeutic implications in asbestos-related diseases.

IT 153436-53-4, AG-1478
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(asbestos-induced phosphorylation of epidermal growth factor receptor is linked to c-fos and apoptosis)
RN 153436-53-4 HCPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

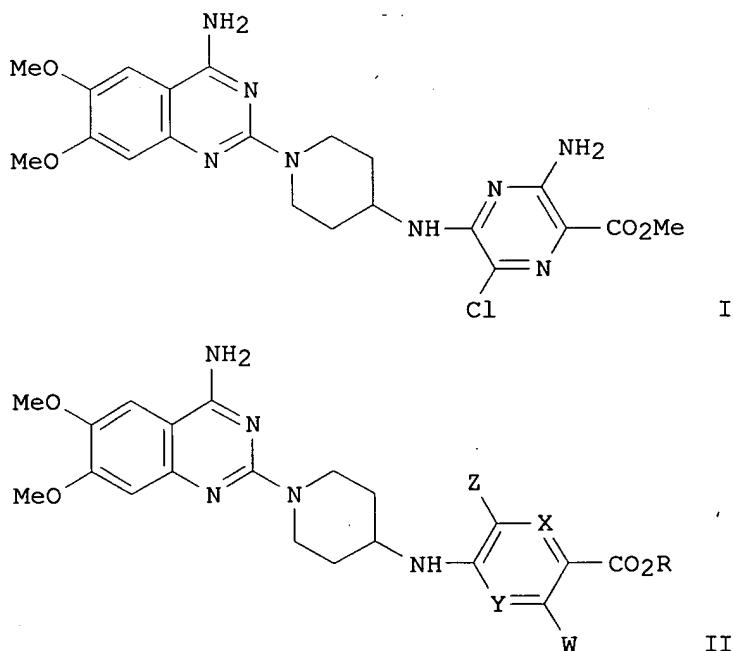
L6 ANSWER 14 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:700927 HCPLUS
 DOCUMENT NUMBER: 132:151765
 TITLE: Synthesis and biological activity of 4-substituted quinazolines
 AUTHOR(S): Abdel-Hamide, S. G.
 CORPORATE SOURCE: Pharmaceutical Chemistry Department, Faculty of Pharmacy, Al-Azhar University, Cairo, Egypt
 SOURCE: Indian Journal of Heterocyclic Chemistry (1999), 9(1), 63-68
 CODEN: IJCHEI; ISSN: 0971-1627
 PUBLISHER: Prof. R. S. Varma
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A new series of quinazoline derivs. were synthesized using the corresponding 4-chloro-2-phenyl-6-iodo-quinazoline as starting material. On screening, some of them were found to exhibit good antibacterial activity.
 IT 257624-35-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and biol. activity of 4-substituted quinazolines)
 RN 257624-35-4 HCPLUS
 CN Ethanone, 1-[4-[(6-iodo-2-phenyl-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:653031 HCPLUS
 DOCUMENT NUMBER: 132:64231
 TITLE: Structure-activity relationships of novel
 2-substituted quinazoline antibacterial agents
 AUTHOR(S): Kung, Pei-Pei; Casper, Martin D.; Cook, Kimberley L.;
 Wilson-Lingardo, Laura; Risen, Lisa M.; Vickers,
 Timothy A.; Ranken, Ray; Blyn, Lawrence B.; Wyatt,
 Jacqueline R.; Cook, P. Dan; Ecker, David J.
 CORPORATE SOURCE: Ibis Therapeutics a Division of Isis Pharmaceuticals
 and Medicinal Chemistry, Isis Pharmaceuticals,
 Carlsbad, CA, 92008, USA
 SOURCE: Journal of Medicinal Chemistry (1999), 42(22),
 4705-4713
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB High-throughput screening of inhouse compound libraries led to the discovery of a novel antibacterial agent, pyrazinyl quinazoline compound I (MIC: 12-25 μM against *S. pyogenes*). In an effort to improve the activity of this active compound, a series of 2-substituted quinazolines, e.g., II ($\text{X} = \text{N}$, CH , $\text{Z} = \text{Cl}$, H , NO_2 , $\text{W} = \text{NH}_2$, H , $\text{R} = \text{Me}$, CMe_3 , H) was synthesized and evaluated in several antibacterial assays. One such compound, I ($\text{X} = \text{Y} = \text{CH}$, $\text{Z} = \text{W} = \text{R} = \text{H}$) (III) displayed improved broad-spectrum antibacterial activity against a variety of bacterial strains. This mol. also inhibited transcription/translation of bacterial RNA, suggesting a mechanism for its antibiotic effects. Structure-activity relationship studies of III led to

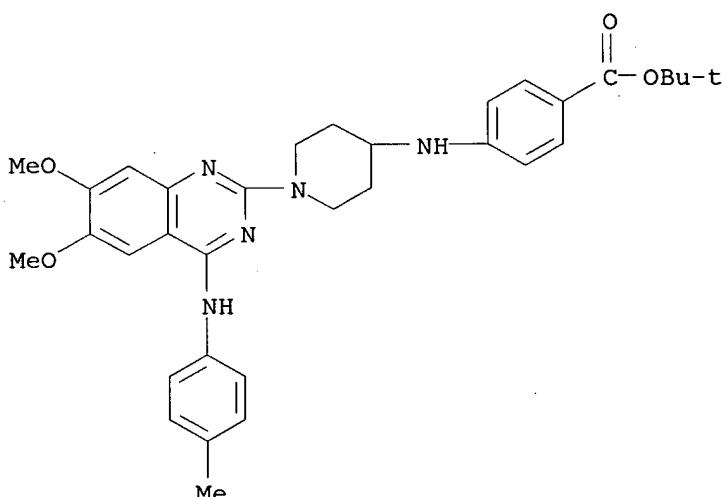
the synthesis of another 24 compds. Although some of these mols. were found to be active in bacterial growth assays, none were as potent as III. Compound III was tested for its ability to cure a systemic K. pneumonia infection in the mouse and displayed moderate effects compared with a control antibiotic, gentamycin.

IT 253192-02-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, antibacterial activity, and structure-activity relationship of quinazolines)

RN 253192-02-8 HCPLUS

CN Benzoic acid, 4-[[1-[6,7-dimethoxy-4-[(4-methylphenyl)amino]-2-quinazolinyl]-4-piperidinyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:622744 HCPLUS

DOCUMENT NUMBER: 131:309757

TITLE: Targeting Janus kinase 3 in mast cells prevents immediate hypersensitivity reactions and anaphylaxis

AUTHOR(S): Malaviya, Ravi; Zhu, DeMin; Dibirdik, Ilker; Uckun, Fatih M.

CORPORATE SOURCE: Department of Allergy, Hughes Institute, St. Paul, MN, 55113, USA

SOURCE: Journal of Biological Chemistry (1999), 274(38), 27028-27038

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Janus kinase 3 (JAK3), a member of the Janus family protein-tyrosine kinases, is expressed in mast cells, and its enzymic activity is enhanced by IgE receptor/Fc ϵ RI crosslinking. Selective inhibition of JAK3 in mast cells with 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) blocked the phospholipase C activation, calcium mobilization,

and activation of microtubule-associated protein kinase after IgE receptor/Fc ϵ RI crosslinking. Treatment of IgE-sensitized rodent as well as human mast cells with WHI-P131 effectively inhibited the activation-associated morphol. changes, degranulation, and proinflammatory mediator release after specific antigen challenge without affecting the functional integrity of the distal secretory machinery. In vivo administration of the JAK3 inhibitor WHI-P131 prevented mast cell degranulation and development of cutaneous as well as systemic fatal anaphylaxis in mice at nontoxic dose levels. Thus, JAK3 plays a pivotal role in IgE receptor/Fc ϵ RI-mediated mast cell responses, and targeting JAK3 with a specific inhibitor, such as WHI-P131, may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions.

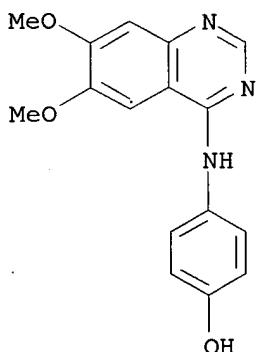
IT 202475-60-3, WHI-P131

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeting JAK3 in mast cells prevents immediate hypersensitivity reactions and anaphylaxis)

RN 202475-60-3 HCPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:547970 HCPLUS

DOCUMENT NUMBER: 131:295318

TITLE: Tyrophostins that suppress the growth of human papilloma virus 16-immortalized human keratinocytes
Ben-Bassat, H.; Rosenbaum-Mitrani, S.; Hartzstark, Z.; Levitzki, R.; Chaouat, M.; Shlomai, Z.; Klein, B. Y.; Kleinberger-Doron, N.; Gazit, A.; Tsvieli, R.; Levitzki, A.

CORPORATE SOURCE: Laboratory of Experimental Surgery, Jerusalem, Israel
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(3), 1442-1457

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human papilloma virus 16 (HPV16) is considered to be the causative agent for cervical cancer, which ranks second to breast cancer in women's malignancies. In an attempt to develop drugs that inhibit the malignant

transformation of HPV16-immortalized epithelial cells, we examined the effect of tyrphostins on such cells. We examined the effect of tyrphostins from four different families on the growth of HPV16-immortalized human keratinocytes (HF-1) cells. We found that they alter their cell cycle distribution, their morphol., and induce cell death by apoptosis. The effects of tyrphostins on HF-1 cells are different from their effects on normal keratinocytes. Growth suppression by AG555 and AG1478 is accompanied by 30% apoptosis in HF-1 cells, but this is not observed in normal keratinocytes. Tyrphostin treatment produces distinctive morphol. changes in HF-1 cells and in normal keratinocytes; however, the culture organization of normal keratinocytes is less disrupted. These differential effects of the tyrphostins on HPV16-immortalized keratinocytes compared with their effects on normal keratinocytes suggests that these compds. are suitable candidates for the treatment of papilloma. Previous and present results indicate that group 1 tyrphostins, which inhibit Cdk2 activation, and group 2 tyrphostins, represented by AG1478, a potent epidermal growth factor receptor kinase inhibitor, induce cell cycle arrest; and, in the case of HF-1 cells, apoptosis and differentiation. Cells accumulate in the G1 phase of the cell cycle at the expense of S and G2 + M. These compds. block the growth of normal keratinocytes without inducing apoptosis or differentiation, causing them to accumulate in G1. AG17, which belongs to group 4, exerts its antiproliferative effect mainly by increasing the fractions of cells in G1 with a concomitant decrease in the fraction of cells in S and G2 + M.

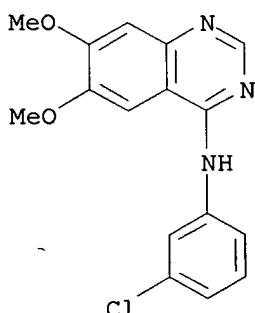
IT 153436-53-4, AG 1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tyrphostins suppress growth of human papilloma virus 16-immortalized human keratinocytes)

RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

41

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:537286 HCAPLUS

DOCUMENT NUMBER: 132:58929

TITLE: In vitro modulation of cyst formation by a novel tyrosine kinase inhibitor

AUTHOR(S): Sweeney, William E.; Futey, Lidia; Frost, Phillip; Avner, Ellis D.

CORPORATE SOURCE: Department of Pediatrics, Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, OH, USA

SOURCE: Kidney International (1999), 56(2), 406-413
 CODEN: KDYIA5; ISSN: 0085-2538

PUBLISHER: Blackwell Science, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

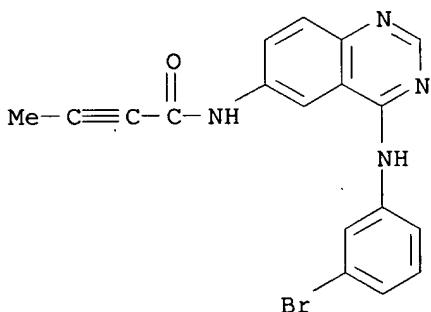
AB Recessively transmitted polycystic kidney disease (PKD) in many murine models is characterized by the initial formation of proximal tubular cysts (stage 1), followed by growth and enlargement of renal collecting tubule (CT) cysts (stage 2). Previous studies have reported that stage 1 cyst formation and growth could be manipulated in vitro by using embryonic kidney explants and newborn explant microslices in organ culture. Microslices of postnatal kidneys cultured on Transwell tissue culture inserts allow exptl. manipulation of stage 2 CT cyst development and growth. This system was used to test a potential therapeutic compound for treatment of PKD. This compound, EKI-785, modulates altered epidermal growth factor receptor (EGFR) expression in CT cysts by inhibition of EGFR autophosphorylation. The present expts. demonstrated that: (a) minor modifications of the previously described organ culture system permit successful culture of more mature renal tissue, and (b) cystic explants treated with EGF and EKI-785 demonstrated a marked reduction in CT cystic lesions compared with cystic explants treated with EGF alone. This study suggests that pharmacol. strategies can be used to decrease EGFR tyrosine kinase activity and CT cyst formation and enlargement in murine PKD.

IT 194423-06-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (cyst formation modulation by tyrosine kinase inhibitor EKI-785)

RN 194423-06-8 HCPLUS

CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:487527 HCPLUS

DOCUMENT NUMBER: 131:111456

TITLE: Use of specific phosphodiesterase inhibitors for increasing sperm motility

INVENTOR(S): Taher, Akmal; Meyer, Markus; Forssmann, Wolf-Georg

PATENT ASSIGNEE(S): Haemopep Pharma G.m.b.H., Germany

SOURCE: Ger. Offen., 8 pp.

CODEN: GWXXBX

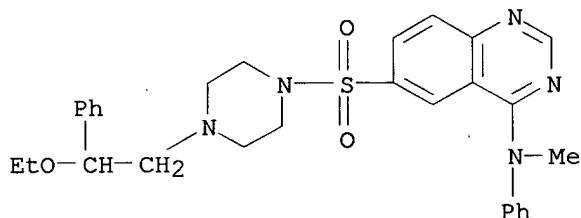
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|------------------|----------|
| DE 19801438 | A1 | 19990729 | DE 1998-19801438 | 19980116 |
| PRIORITY APPLN. INFO.: | | | | |
| AB Inhibitors of phosphodiesterases I, III, and IV stimulate sperm motility and are useful in artificial insemination, in vitro fertilization, intracytoplasmic sperm injection, and diagnosis and treatment of asthenozoospermia and related fertility disorders. Thus, vinpocetine, a phosphodiesterase I inhibitor, at 10-6M increased the number of motile sperm from asthenozoospermic patients from 30-35 to 65%. | | | | |
| IT 81871-31-0, HA-558 | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) | | | |
| | (specific phosphodiesterase inhibitors for increasing sperm motility) | | | |
| RN 81871-31-0 HCAPLUS | | | | |
| CN Piperazine, 1-(2-ethoxy-2-phenylethyl)-4-[[4-(methylphenylamino)-6-quinazolinyl]sulfonyl]- (9CI) (CA INDEX NAME) | | | | |



L6 ANSWER 20 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:473371 HCAPLUS
 DOCUMENT NUMBER: 131:284748
 TITLE: Specific inhibitors of platelet-derived growth factor or epidermal growth factor receptor tyrosine kinase reduce pulmonary fibrosis in rats
 AUTHOR(S): Rice, Annette B.; Moomaw, Cindy R.; Morgan, Daniel L.; Bonner, James C.
 CORPORATE SOURCE: Laboratories of Pulmonary Pathobiology, National Institute of Environmental Health Sciences, Research Triangle Park, 27709, USA
 SOURCE: American Journal of Pathology (1999), 155(1), 213-221
 CODEN: AJPAA4; ISSN: 0002-9440
 PUBLISHER: American Society for Investigative Pathology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The proliferation of myofibroblasts is a central feature of pulmonary fibrosis. In this study we have used tyrosine kinase inhibitors of the tyrphostin class to specifically block autophosphorylation of the platelet-derived growth factor receptor (PDGF-R) or epidermal growth factor receptor (EGF-R). AG1296 specifically inhibited autophosphorylation of PDGF-R and blocked PDGF-stimulated [³H]thymidine uptake by rat lung myofibroblasts in vitro. AG1478 was demonstrated as a selective blocker of EGF-R autophosphorylation and inhibited EGF-stimulated DNA synthesis in vitro. In a rat model of pulmonary fibrosis caused by intratracheal instillation of vanadium pentoxide (V2O5), i.p. delivery of 50 mg/kg AG1296 or AG1478 in dimethylsulfoxide 1 h before V2O5 instillation and again 2 days after instillation reduced the number of epithelial and mesenchymal cells incorporating bromodeoxyuridine

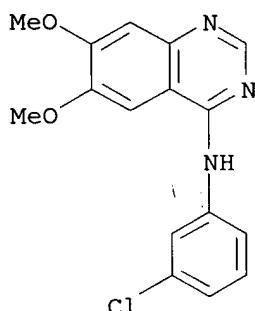
(Brdu) by .apprx.50% at 3 and 6 days after instillation. V205 instillation increased lung hydroxyproline fivefold 15 days after instillation, and AG1296 was more than 90% effective in preventing the increase in hydroxyproline, whereas AG1478 caused a 50% to 60% decrease in V205-stimulated hydroxyproline accumulation. These data provide evidence that PDGF and EGF receptor ligands are potent mitogens for collagen-producing mesenchymal cells during pulmonary fibro-genesis, and targeting tyrosine kinase receptors could offer a strategy for the treatment of fibrotic lung diseases.

IT 153436-53-4, AG1478

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(specific inhibitors of platelet-derived growth factor or epidermal growth factor receptor tyrosine kinase reduce pulmonary fibrosis in rats)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

40

THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:471865 HCPLUS

DOCUMENT NUMBER: 131:125463

TITLE: Method of treating polycystic kidney disease with a quinazoline derivative, and preparation thereof

INVENTOR(S): Frost, Philip

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 10 pp.

CODEN: USXXAM

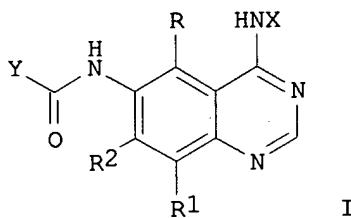
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|------------|-----------------|------------|
| ----- | --- | ----- | ----- | ----- |
| US 5929080 | A | 19990727 | US 1998-63452 | 19980421 |
| PRIORITY APPLN. INFO.: | | | US 1997-45679P | P 19970506 |
| OTHER SOURCE(S): | MARPAT | 131:125463 | | |
| GI | | | | |



AB A method for treating or inhibiting polycystic kidney disease in a mammal in need thereof comprises administering I [X = (substituted) Ph; R, R1 = H, halo, alkyl, alkoxy, OH, CF3; R2 = H, alkyl, alkoxy, OH, CF3; Y = R3C.tpbond.C, (R3)2C=C(R3), etc. (R3 = H, alkyl, carboxy, carboalkoxy, Ph, carboalkyl)] or a pharmaceutically acceptable salt thereof. Preparation of e.g. N-[4-((3-bromophenyl)amino)-6-quinazolinyl]-2-butynamide is described.

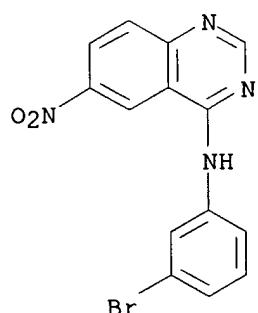
IT 169205-77-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(préparation et réaction; quinazolinamine derivative preparation for polycystic kidney disease treatment)

RN 169205-77-0 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6-nitro- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 22 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:451283 HCPLUS

DOCUMENT NUMBER: 131:102287

TITLE: Preparation of quinazolinylamines and analogs as protein tyrosine kinase inhibitors

INVENTOR(S): Cockerill, George Stuart; Lackey, Karen Elizabeth

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 145 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

| | | | | |
|---------------------|---|----------|---------------|------------|
| WO 9935132 | A1 | 19990715 | WO 1999-GB76 | 19990111 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 9919786 | A | 19990726 | AU 1999-19786 | 19990111 |
| ORITY APPLN. INFO.: | | | GB 1998-575 | A 19980112 |
| | | | WO 1999-GB76 | W 19990111 |

OTHER SOURCE(S): MARPAT 131:102287

GI

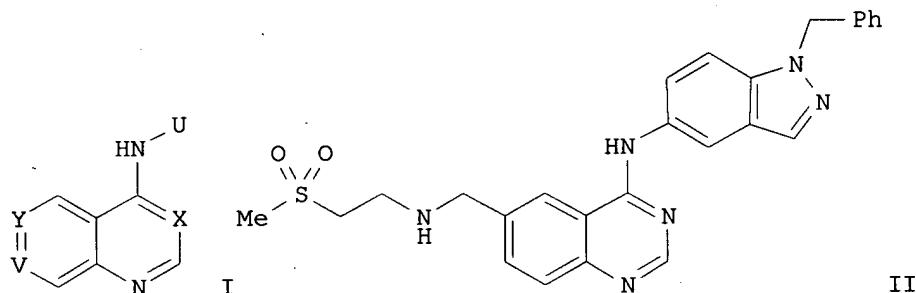
AU 1999-19786

19990111

GB 1998-575

A 19980112

W 19990111



AB Substituted heteroarom. compds. I are prepared [wherein X = N or CH; Y = CR1 and V = N; or Y = N and V = CR1; or Y = CR1 and V = CR2; or Y = CR2 and V = CR1; R1 = Q-M-, wherein M = C1-5 alkylene where any C atom not immediately adjacent to Q may be replaced by O, S, or NR6; Q = wide variety of groups; R2 = H, halo, OH, alkyl, alkoxy, (di)alkylamino; U = Ph, pyridyl, pyrimidinyl, imidazolyl, or 9- or 10-membered bicyclic heterocyclyl containing 1-2 N atoms and 0-1 addnl. O, N, or S; U is substituted by R3, where R3 = benzyl, halobenzyl, pyridylmethyl, pyridylmethoxy, PhO, PhSO₂, (un)substituted phthalimido; R6 = H, alkyl]. Twelve examples and a variety of intermediates were prepared. For instance, 4-chloro-6-iodoquinazoline was aminated in the 4-position with 5-amino-1-benzyl-1H-indazole, followed by Pd-catalyzed carbonylation, to give 4-[(1-benzyl-1H-indazol-5-yl)amino]quinazoline-6-carbaldehyde. This underwent reductive amination by MeSO₂CH₂CH₂NH₂ and a reducing agent such as NaBH(OAc)₃, to give title compound II.HCl. In an EGFr phosphorylation assay, II.HCl had an IC₅₀ of <0.10 μM.

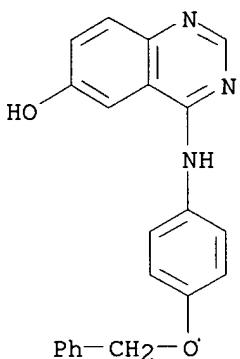
IT 179246-81-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of quinazolinylamines and analogs as protein tyrosine kinase inhibitors)

RN 179246-81-2 HCAPLUS

CN 6-Quinazolinol, 4-[[4-(phenylmethoxy)phenyl]amino]- (9CI) (CA INDEX NAME)

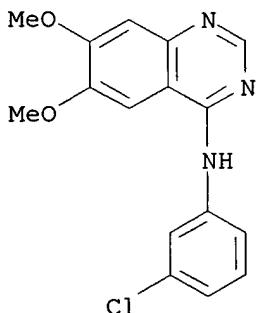


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:443061 HCPLUS
 DOCUMENT NUMBER: 131:226472
 TITLE: Regulation of Na⁺-K⁺-2Cl⁻ cotransport by protein phosphorylation in ferret erythrocytes
 AUTHOR(S): Flatman, Peter W.; Creanor, James
 CORPORATE SOURCE: Membrane Biology Group, Department of Biomedical Sciences, University Medical School, Edinburgh, EH8 9AG, UK
 SOURCE: Journal of Physiology (Cambridge, United Kingdom) (1999), 517(3), 699-708
 CODEN: JPHYA7; ISSN: 0022-3751
 PUBLISHER: Cambridge University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Na⁺-K⁺-2Cl⁻ cotransport in ferret erythrocytes was measured as the bumetanide-sensitive uptake of 86Rb. The resting cotransport rate was high but could be increased threefold by treating erythrocytes with calyculin A, a potent inhibitor of serine/threonine phosphatases. Twenty nanomolar was sufficient to maximally and rapidly (within 4 min) stimulate transport. The effects of several kinase inhibitors were tested. High concns. of K-252a, K-252b, calphostin C and hypericin caused less than 20% inhibition. Staurosporine (IC₅₀, 0.06 μM) and 4-amino-5-(4-methylphenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine (PP1; IC₅₀, 2.5 μM) were more potent but still only partially (40-50%) inhibited transport, an effect mimicked by reducing ionized intracellular Mg²⁺ concentration to submicromolar levels. Genistein may inhibit all transport at a sufficiently high dose (IC₅₀, 0.36 mM) perhaps by directly inhibiting the transporter. Staurosporine, PP1 and the removal of Mg²⁺ all prevented subsequent stimulation by calyculin A, and all inhibited calyculin-stimulated transport by 20-30%. The effects of staurosporine, PP1 and Mg²⁺ removal were not additive. The phosphatase that dephosphorylates the cotransporter is probably Mg²⁺ (or possibly Ca²⁺ or Mn²⁺) sensitive and not the target for calyculin A. The data suggest that this phosphatase is inhibited by phosphorylation, and that it is the regulation of this process which is affected by calyculin A and the kinase inhibitors tested here. Phosphorylation of the phosphatase is probably regulated by members of the Src family of tyrosine kinases.
 IT 153436-53-4, AG1478
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (effects of inhibitors of kinases and phosphatases on Na⁺-K⁺-2Cl⁻

cotransport in ferret erythrocytes)

RN 153436-53-4 HCAPLUS
 CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX
 NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:428003 HCAPLUS
 DOCUMENT NUMBER: 131:295193
 TITLE: Structure-based design of specific inhibitors of janus kinase 3 as apoptosis-inducing antileukemic agents
 AUTHOR(S): Sudbeck, Elise A.; Liu, Xing-Ping; Narla, Rama Krishna; Mahajan, Sandeep; Ghosh, Sutapa; Mao, Chen; Uckun, Fatih M.
 CORPORATE SOURCE: Parker Hughes Cancer Center, Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Clinical Cancer Research (1999), 5(6), 1569-1582
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A novel homol. model of the kinase domain of Janus kinase (JAK) 3 was used for the structure-based design of dimethoxyquinazoline compds. with potent and specific inhibitory activity against JAK3. The active site of JAK3 in this homol. model measures roughly 8 Å + 11 Å + 20 Å, with a volume of .apprx.530 Å³ available for inhibitor binding. Modeling studies indicated that 4-(phenylamino)-6,7-dimethoxyquinazoline (WHI-258) (I) would likely fit into the catalytic site of JAK3 and that derivs. of I that contain an OH group at the 4' position of the Ph ring would more strongly bind to JAK3 because of added interactions with Asp-967, a key residue in the catalytic site of JAK3. These predictions were consistent with docking studies indicating that compds. containing a 4-OH group, WHI-P131 [4-((4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P154 [4-((3-bromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P97 [4-((3,5-dibromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], were likely to bind favorably to JAK3, with estimated Kis ranging from 0.6 to 2.3 µM. These compds. inhibited JAK3 in immune complex kinase assays in a dose-dependent fashion. In contrast, compds. lacking the 4-OH group, WHI-P79 [4-((3-bromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P111 [4-((3-bromo-4-methylphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P112 [4-((2,5-dibromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P132 [4-((2-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P258 [4-(phenylamino)-6,7-dimethoxyquinazoline], were predicted to bind less strongly, with estimated Kis ranging from 28 to 72 µM. These compds. did not show any

significant JAK3 inhibition in kinase assays. Furthermore, the lead dimethoxyquinazoline compound, WHI-P131, which showed potent JAK3-inhibitory activity (IC₅₀ of 78 μM), did not inhibit JAK1 and JAK2, the ZAP/SYK family tyrosine kinase SYK, the TEC family tyrosine kinase BTK, the SRC family tyrosine kinase LYN, or the receptor family tyrosine kinase insulin receptor kinase, even at concns. as high as 350 μM. WHI-P131 induced apoptosis in JAK3-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma (M24-MET) or squamous carcinoma (SQ20B) cells. Leukemia cells were not killed by dimethoxyquinazoline compds. that were inactive against JAK3. WHI-P131 inhibited the clonogenic growth of JAK3-pos. leukemia cell lines DAUDI, RAMOS, LC1;19, NALM-6, MOLT-3, and HL-60 (but not JAK3-neg. BT-20 breast cancer, M24-MET melanoma, or SQ20B squamous carcinoma cell lines) in a concentration-dependent fashion. Potent

and

specific inhibitors of JAK3 such as WHI-P131 may provide the basis for the design of new treatment strategies against acute lymphoblastic leukemia, the most common form of childhood cancer.

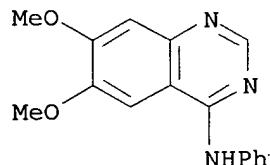
IT 21561-09-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(structure-based design of specific inhibitors of janus kinase 3 as apoptosis-inducing antileukemic agents)

RN 21561-09-1 HCPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:412113 HCPLUS

DOCUMENT NUMBER: 131:167191

TITLE: In vivo evaluation of the biodistribution of ¹¹C-labeled PD153035 in rats without and with neuroblastoma implants

AUTHOR(S): Fredriksson, Anna; Johnstrom, Peter; Thorell, Jan-Olov; Von Heijne, Gustav; Hassan, Moustapha; Eksborg, Staffan; Kogner, Per; Borgstrom, Per; Ingvar, Martin; Stone-Elander, Sharon

CORPORATE SOURCE: Karolinska Pharmacy, Karolinska Hospital and Institute, Stockholm, S-17176, Swed.

SOURCE: Life Sciences (1999), 65(2), 165-174
CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The biodistribution of ¹¹C-labeled 4-(3-bromoanilino)-6,7-dimethoxyquinazoline, an inhibitor of the epidermal growth factor (EGF) receptor tyrosine kinase, has been evaluated in vivo in rats using positron emission tomog. (PET). Time-activity data obtained after i.v. administration in one rat revealed that the radiotracer rapidly cleared from plasma with subsequent uptake in major organs of the body (brain,

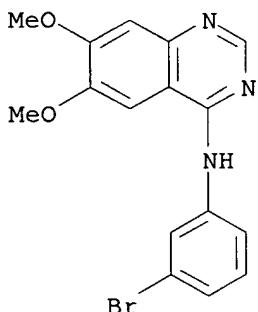
heart, liver, gastrointestinal tract and bladder). Uptake in proliferating tissue in rats with human neuroblastoma xenografts indicate that [O-11C-methyl]PD153035 shows promise as a new agent for in vivo imaging of tumors with PET.

IT 212211-01-3

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (biodistribution of 11C-labeled PD153035 in rats without and with neuroblastoma implants)

RN 212211-01-3 HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6(or 7)-methoxy-7(or 6)-(methoxy-11C)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 26 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:404065 HCAPLUS

DOCUMENT NUMBER: 131:179230

TITLE: A quantitative HPLC detection method for WHI-P154 [4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline]

AUTHOR(S): Chen, C. L.; Narla, R. K.; Liu, X. P.; Uckun, F. M.
CORPORATE SOURCE: Parker Hughes Cancer Center, Department of Molecular Pharmacology, Hughes Institute, St. Paul, MN, 55113, USASOURCE: Journal of Liquid Chromatography & Related Technologies (1999), 22(11), 1771-1783
CODEN: JLCTFC; ISSN: 1082-6076

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB WHI-P154 [4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7 dimethoxyquinazoline] is a novel anti-tumor agent with unique cytotoxic activity against human glioblastoma cells (Clin. Cancer. Res. 4:1405-1414, 1998). Further development of WHI-P154 will require detailed pharmacodynamic studies in preclin. animal models. Therefore, we established a sensitive and accurate high performance liquid chromatog. (HPLC)-based quant. detection method for WHI-P154. This method allows the measurement of WHI-P154 levels in plasma, as well as in target human glioblastoma cells. Plasma and cell lysates were extracted with chloroform, dried with nitrogen gas and reconstituted in methanol: water (9:1, volume/volume). An aliquot was injected into a Hewlett Packard HPLC system employing a 250+4 mm Lichrospher 100, RP-18 (5 μ m) anal. column in conjunction with a 4+4 mm Lichrospher 100, RP-18 (5 μ m) guard column. The eluted compds. were detected by a diode array detector set at a wavelength of 335 nm. Acetonitrile/water containing 0.1% trifluoroacetic acid and 0.1%

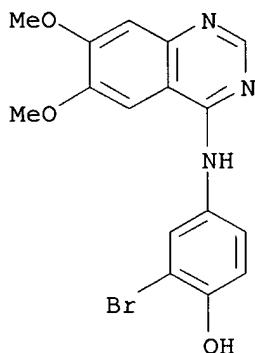
triethylamine (28:72, volume/volume) was used as a mobile phase. The average extraction recovery of WHI-P154 was 78.3% for plasma and 96.0% for U373 human glioblastoma cells. The assay was linear ($r>0.999$) within the concentration range of 0.1-20 μM in 100 μL plasma and within the quantity range of 0.025-5 nmol per 2.5 million U373 glioblastoma cells. The intra- and inter-assay variabilities were less than 6% and the lowest detection limit of WHI-P154 was 0.05 μM in plasma and 0.01 nmol in U373 cells, resp. The practical utility of this new HPLC method was confirmed in pilot pharmacokinetic studies using rats as well as cellular uptake studies using U373 human glioblastoma cells.

IT 211555-04-3, WHI-P154

RL: ANT (Analyte); ANST (Analytical study)
(quant. HPLC detection method for WHI-P154)

RN 211555-04-3 HCPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 27 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:400919 HCPLUS

DOCUMENT NUMBER: 131:67806

TITLE: Inhibition of epidermal-growth-factor-receptor-dependent signalling by tyrphostins A25 and AG1478 blocks growth and induces apoptosis in colorectal tumor cells in vitro

AUTHOR(S): Partik, Gerda; Hochegger, Karin; Schorkhuber, Michaela; Marian, Brigitte

CORPORATE SOURCE: Inst. Tumor Biology-Cancer Res., Univ. Vienna, Vienna, A-1090, Austria

SOURCE: Journal of Cancer Research and Clinical Oncology (1999), 125(7), 379-388

CODEN: JCROD7; ISSN: 0171-5216

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Growth effects of tyrphostins A25 and AG1478 on colorectal tumor cells (HT29/H11, SW480, T84, and VACO235) were investigated. Both tyrphostins inhibited DNA synthesis and induced apoptosis in tumor cells with different activity. A25 displayed strong selectivity for the cell lines expressing high levels of epidermal growth factor, HT29/H11 and SW480. Inhibition of DNA synthesis was efficient in all cells except T84, and the apoptotic index increased 2-5-fold. AG1478 was highly effective in all cell lines. It caused cell loss in VACO235 adenoma cells at concns. lower

than those necessary to inhibit 5-bromo-2'-deoxyuridine incorporation. Induction of apoptosis was more efficient with AG1478 than with A25. Insulin-like growth factor rescued cells exposed to suboptimal amts. of AG1478. Both tyrphostins inhibited phosphorylation of the epidermal growth factor receptor and addnl. proteins. AG1478 induced expression of Bak and down-regulated Bcl-2.

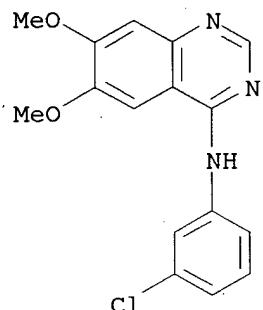
IT 153436-53-4, Tyrphostin AG 1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tyrphostins A25 and AG1478 inhibited epidermal growth factor receptor-dependent signalling and induced apoptosis in colorectal tumor)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:396030 HCPLUS

DOCUMENT NUMBER: 131:223160

TITLE: Growth inhibition of nasopharyngeal carcinoma cells by EGF receptor tyrosine kinase inhibitors

AUTHOR(S): Sun, Yi; Fry, David W.; Vincent, Patrick; Nelson, James M.; Elliott, William; Leopold, Wilbur R.

CORPORATE SOURCE: Department of Molecular Biology, Division of Warner-Lambert Company, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA

SOURCE: Anticancer Research (1999), 19(2A), 919-924

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nasopharyngeal carcinoma (NPC) is a malignancy of epithelial origin occurring with a high incidence in southern China and southeast Asia. Radiotherapy is the main treatment modality for NPC. No effective chemotherapy is available. Since prevention of EGF/EGFR binding by an EGFR specific monoclonal antibody suppressed the growth of NPC xenografts, we examined potential anti-NPC activity by a group of specific inhibitors of the EGFR family of tyrosine kinases. We found that HONE-T1 NPC cells expressed high levels of EGFR tyrosine kinase activity upon stimulation by EGF. The receptor tyrosine kinase activity was specifically inhibited by either reversible (PD 158780) or irreversible (PD 168393) inhibitors specific for EGFR family tyrosine kinases. This inhibition led to a dose-dependent suppression of anchorage-independent growth as determined by

soft agar assays. A structural analog (PD 159805) with no inhibitory activity against EGFR tyrosine kinase had no effect on HONE-T1 cell growth in agar. Furthermore, growth of HONE-T1 xenografts in SCID mice was also inhibited by treatment with PD 158780 and PD 168393. This data provides an appealing application of EGFR tyrosine kinase inhibitors for the treatment of nasopharyngeal carcinomas.

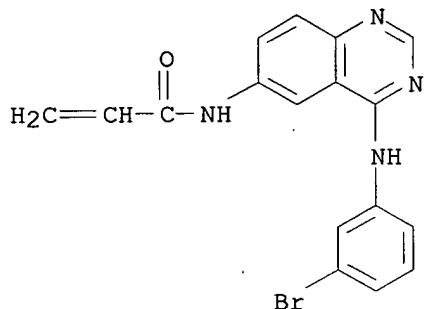
IT 194423-15-9, PD 168393

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(growth inhibition of nasopharyngeal carcinoma cells by EGF receptor tyrosine kinase inhibitors)

RN 194423-15-9 HCPLUS

CN 2-Propenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

26

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:341446 HCPLUS

DOCUMENT NUMBER: 131:96898

TITLE: Quantitative high-performance liquid chromatographic method for pharmacokinetic studies of the potent mast cell inhibitor 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline (WHI-P131)

AUTHOR(S): Chen, Chun-Lin; Malaviya, Ravi; Chen, Hao; Liu, Xing-Ping; Uckun, Fatih M.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, Hughes Institute, St. Paul, MN, USA

SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 727(1 + 2), 205-212
CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel quinazoline derivative 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline (WHI-P131) has recently been identified as a potent mast cell inhibitor capable of preventing IgE/antigen-induced cutaneous as well as systemic fatal anaphylaxis in mice. Here, the authors describe a sensitive high-performance liquid chromatog. (HPLC)-based quant. detection method for measurement of WHI-P131 levels in plasma as well as in target mast cells. The average extraction recovery for WHI-P131 was 88.4% for plasma and

75.7% for RBL-2H3 mast cell lysates. Good linearity ($r>0.999$) was observed throughout the concentration range of 0.1-20 μM in plasma and 0.01-5 nmol in 5·10⁶ cells (0.5-238 μM per cell) for WHI-P131. Intra- and

interassay variabilities were <7% and the lowest detection limit of WHI-P131 was 0.05 μM in plasma and 0.005 nmol in 5 million cells, resp., at a signal-to-noise ratio of .apprx.2. The practical utility of this new HPLC method was confirmed in a pilot pharmacokinetic study in BALB/c mice as well as in a cellular drug uptake and disposition study in RBL-2H3 mast cells. After i.p. administration of a non-toxic 40 mg/kg bolus dose of WHI-P131, the estimated maximum plasma concentration was 92.7 μM , which

is .apprx.1-log higher than the effective in vitro mast cell inhibitory concns. of WHI-P131. The drug absorption was rapid with an absorption half-life of only 2.9 min and the estimated time to reach the maximum plasma concentration was 8.3 min. WHI-P131 was cleared with an apparent systemic clearance rate of 2586 mL/h/kg and an elimination half-life of 1.8 h. An intracellular exposure level (AUC) of 55 $\mu\text{M}\cdot\text{h}$ was obtained after in vitro treatment of RBL-2H3 mast cells with WHI-P131 at a 33.6 μM final concentration in culture medium. The availability of the described quant.

HPLC detection method for WHI-P131 provides the basis for further development of WHI-P131 as an anti-allergic drug through detailed pharmacodynamic studies in preclin. animal models.

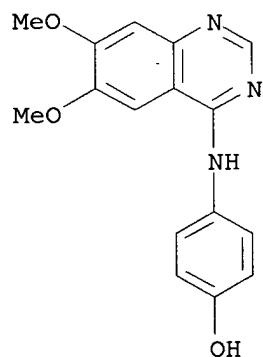
IT 202475-60-3, WHI-P131

RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(high-performance liquid chromatog. method for pharmacokinetic studies of WHI-P131)

RN 202475-60-3 HCPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 30 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:298066 HCPLUS

DOCUMENT NUMBER: 131:111006

TITLE: Enhancement of chemosensitivity and programmed cell death by tyrosine kinase inhibitors correlates with EGFR expression in non-small cell lung cancer cells

AUTHOR(S): Lei, Wendong; Mayotte, Jane E.; Levitt, Mark L.

CORPORATE SOURCE: Lung Cancer Program, Allegheny University of the Health Sciences, Pittsburgh, PA, 15212, USA

SOURCE: Anticancer Research (1999), 19(1A), 221-228

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE:

English

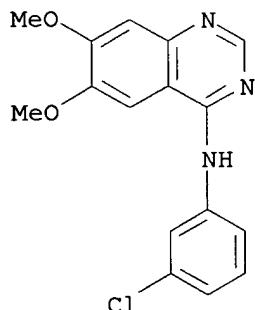
AB Epidermal growth factor receptor (EGFR) is a 170-kD transmembrane glycoprotein with tyrosine kinase activity. Overexpression of the EGFR has been detected in many human cancers, including non-small cell lung cancer (NSCLC), and is correlated with poor prognosis and chemoresistance. The authors investigated the effects of tyrosine kinase inhibitors on chemosensitivity and chemotherapeutic drug-induced programmed cell death in NSCLC cell lines that express different levels of EGFR. NCI-H596 cells, which strongly express EGFR, were more resistant to the growth inhibitory effects of cisplatin, doxorubicin, and etoposide than were NCI-H358 cells, which only weakly express EGFR. Both genistein, a general tyrosine kinase inhibitor, and tyrphostin AG 1478, a tyrosine kinase inhibitor specific for EGFR, inhibited phosphorylation of EGFR in NCI-H596. Combinations of genistein or tyrphostin AG 1478 with cisplatin, doxorubicin, or etoposide enhanced the antiproliferative effects and induced programmed cell death in NCI-H596 cells whereas no such additive effects were observed in NCI-H358 cells. The programmed cell death induced by these agents involved CPP32-mediated PARP cleavage and DNA fragmentation. These results indicate that tyrosine kinase inhibitors in combination with chemotherapeutic drugs may prove to be a viable therapeutic strategy for the treatment of those types of NSCLC that demonstrate strong expression of EGFR.

IT 153436-53-4, Tyrphostin AG 1478

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of chemosensitivity and programmed cell death by tyrosine kinase inhibitors correlates with EGFR expression in non-small cell lung cancer cells)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

57

THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 31 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:296163 HCPLUS

DOCUMENT NUMBER: 131:31885

TITLE: Functionalization by metalation of the benzene moiety of benzodiazines. Determination of structures by long-range ^1H - ^{15}N correlation at natural abundance. Diazines XXV

AUTHOR(S): Chapoulaud, V. Gautheron; Salliot, I.; Ple, N.; Turck, A.; Queguiner, G.

CORPORATE SOURCE: Laboratoire de Chimie Organique Fine et Heterocyclique, UPRES-A 6014, IRCOF-INSA, Mont St Aignan, 76131, Fr.

SOURCE: Tetrahedron (1999), 55(17), 5389-5404

CODEN: TETRAB; ISSN: 0040-4020

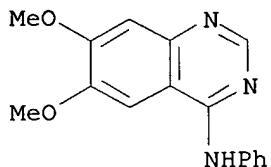
PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 131:31885

AB The first lithiation of the benzene moiety of various quinazolinones, quinoxalines, and phthalazines has been performed. The effects of kind and positions of various directing groups towards the regioselectivity of the metalation have been studied. Unambiguous structure detns. of quinoxaline derivs. have been carried out by applying NMR GHMBC 1H-15N sequence.

IT 21561-09-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (functionalization by metalation of the benzene moiety of benzodiazines)

RN 21561-09-1 HCPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 32 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:284030 HCPLUS
 DOCUMENT NUMBER: 131:82535
 TITLE: Synthesis and antiproliferative properties of 4-aminoquinazoline derivatives as inhibitors of EGF receptor-associated tyrosine kinase activity
 Bouey-Bencteux, Edith; Loison, Cecile; Pommery, Nicole; Houssin, Raymond; Henichart, Jean-Pierre
 Institut de Chimie Pharmaceutique de Lille, Lille, F-59006, Fr.
 AUTHOR(S):
 CORPORATE SOURCE:
 SOURCE: Anti-Cancer Drug Design (1998), 13(8), 893-922
 CODEN: ACDDEA; ISSN: 0266-9536
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The mitogenic action of EGF is mediated by ligand-induced autophosphorylation of the EGF receptor (EGF-R), which is commonly over-expressed in numerous human cancers. Inhibitors of receptor tyrosine kinase (RTK) activity could therefore be considered as effective potential antitumor agents. For this purpose, 4-aminoquinazoline derivs. were prepared and evaluated for their ability to inhibit RTK activity and the autophosphorylation of EGF-R. In addition, these compds. were tested on A431 cell growth to estimate their antiproliferative effect. The results showed that the substituent at the 4-position of the quinazoline ring must be an aromatic amine carrying small lipophilic electron-withdrawing groups on the 3- (or 2-) position of the Ph ring. This aromatic moiety might be far from the quinazoline provided that the linking group is conformationally restricted, such as with piperazine. Hydrophilic and non-aromatic substituents such as morpholine gave completely inactive compds. Introduction of a bulk at the 2-position of the quinazoline ring in 2,4-diaminoquinazolines or tricyclic compds. led to inactive products.

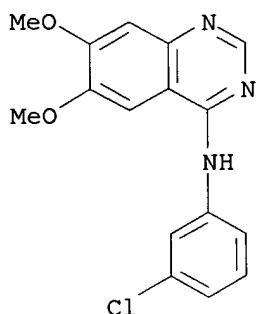
This study reports addnl. structure-activity relationships of a well-characterized series to develop new inhibitors of EGF-R-associated tyrosine kinase activity.

IT 153436-53-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antiproliferative properties of 4-aminoquinazoline derivs. as inhibitors of EGF receptor-associated tyrosine kinase activity)

RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 33 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:278107 HCAPLUS

DOCUMENT NUMBER: 131:44787

TITLE: Tyrosine kinase inhibitors. 15. 4-(Phenylamino)quinazoline and 4-(phenylamino)pyrido[d]pyrimidine acrylamides as irreversible inhibitors of the ATP binding site of the epidermal growth factor receptor

AUTHOR(S): Smaill, Jeff B.; Palmer, Brian D.; Newcastle, Gordon W.; Denny, William A.; McNamara, Dennis J.; Dobrusin, Ellen M.; Bridges, Alexander J.; Zhou, Hairong; Showalter, H. D. Hollis; Winters, R. Thomas; Leopold, Wilbur R.; Fry, David W.; Nelson, James M.; Slintak, Veronika; Elliot, William L.; Roberts, Billy J.; Vincent, Patrick W.; Patmore, Sandra J.

CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (1999), 42(10), 1803-1815

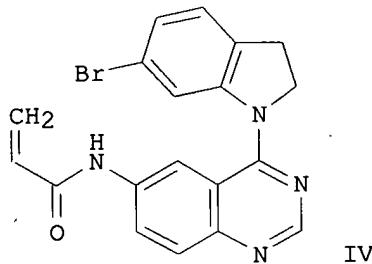
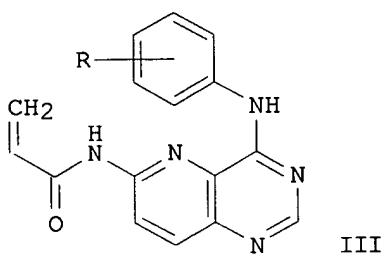
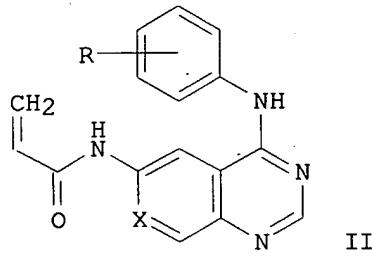
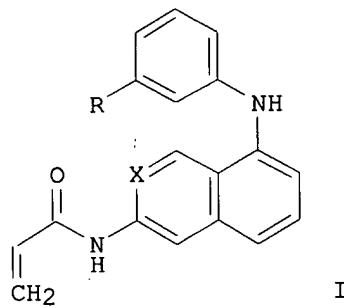
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



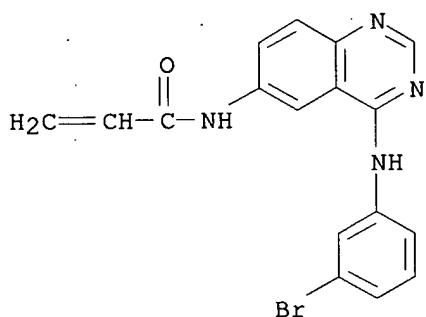
AB A series of 6- and 7-acrylamide derivs. of the 4-(phenylamino)quinazoline and -pyridopyrimidine classes of epidermal growth factor receptor (EGFR) inhibitors, I (R = Br, Cl, Me, X = CH, N), II (R = 3-Br, 3-Cl, 3-Me, 3-CF₃, 3-Br-4-F, 3-Cl-4-F, 4-OPh, 4-OCH₂Ph), III (R = 3-Br, 3-Br-4-F, 3-Cl-4-F), and IV, were prepared from the corresponding amino compds. by reaction with either acryloyl chloride/base or acrylic acid/1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride. All of the 6-acrylamides, but only the parent quinazoline 7-acrylamide, were irreversible inhibitors of the isolated enzyme, confirming that the former are better-positioned, when bound to the enzyme, to react with the critical cysteine-773. Quinazoline, pyrido[3,4-d]pyrimidine, and pyrido[3,2-d]pyrimidine 6-acrylamides were all irreversible inhibitors and showed similar high potencies in the enzyme assay (likely due to titration of the available enzyme). However, the pyrido[3,2-d]pyrimidine analogs were 2-6-fold less potent than the others in a cellular autophosphorylation assay for EGFR in A431 cells. The quinazolines were generally less potent overall toward inhibition of heregulin-stimulated autophosphorylation of erbB2 (in MDA-MB-453-cells), whereas the pyridopyrimidines were equipotent. Selected compds. were evaluated in A431 epidermoid and H125 non-small-cell lung cancer human tumor xenografts. The compds. showed better activity when given orally than i.p. All showed significant tumor growth inhibition (stasis) over a dose range. The poor aqueous solubility of the compds. was a drawback, requiring formulation as fine particulate emulsions.

IT 194423-15-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, antitumor, and tyrosine kinase and EGFR inhibitory activity of (phenylamino)quinazoline and -pyridopyrimidine acrylamides)

RN 194423-15-9 HCAPLUS

CN 2-Propenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 34 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:252227 HCAPLUS

DOCUMENT NUMBER: 131:97069

TITLE: Apoptosis and growth inhibition of head and neck tumor cell line induced by epidermal growth factor receptor tyrosine kinase inhibitor

AUTHOR(S): Faust, R. A.; Tawfic, S.; Davis, A. T.; Ahmed, K.

CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery,
Johns Hopkins University, Baltimore, MD, 21203-6402,
USA

SOURCE: Oral Oncology (1999), 35(3), 290-295

CODEN: EJCCER; ISSN: 1368-8375

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Overexpression of the epidermal growth factor (EGF) receptor, a hallmark of aerodigestive squamous cell carcinoma of the head and neck (SCCHN), correlates with aggressive tumor behavior. There is evidence that SCCHN cells autoactivate their EGF receptors. The receptor has therefore attracted interest as a potential therapeutic target. We tested the in vitro therapeutic efficacy of PD153035 - a potent, specific inhibitor of the tyrosine kinase intrinsic to the EGF receptor - by employing a well-characterized cell line derived from human gingival SCCHN. DNA synthesis and cell number were assayed for growth-inhibitory effects, phosphorylation of the EGF receptor was quantitated by immunoblot, and cell apoptosis was detected by terminal deoxytransferase (TdT)-mediated deoxyuridine triphosphate (dUTP)-biotin nick end labeling (TUNEL) in situ assay. PD153035, at nanomolar concns., inhibited autophosphorylation of the EGF receptor induced by EGF stimulation and the inhibition occurred in a dose-dependent manner. Under the same conditions, PD153035 inhibited cell growth, and induced apoptosis of SCCHN cells in vitro. We conclude that selective inhibition of the EGF receptor tyrosine kinase completely abolishes EGF receptor phosphorylation resulting from receptor stimulation, and results in growth inhibition and apoptosis of SCCHN cells in vitro. By inducing cytostasis and apoptosis, this new class of inhibitors may be of therapeutic value against SCCHN.

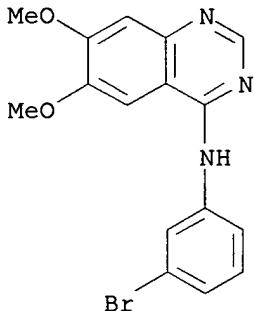
IT 153436-54-5, PD153035

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(apoptosis and growth inhibition of head and neck tumor cell line induced by EGF receptor tyrosine kinase inhibitor)

RN 153436-54-5 HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 35 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:242184 HCAPLUS

DOCUMENT NUMBER: 131:72658

TITLE: Genetic and Biochemical Evidence for a Critical Role of Janus Kinase (JAK)-3 in Mast Cell-Mediated Type I Hypersensitivity Reactions

AUTHOR(S): Malaviya, Ravi; Uckun, Fatih M.

CORPORATE SOURCE: Department of Allergy, Hughes Institute, St. Paul, MN, USA

SOURCE: Biochemical and Biophysical Research Communications (1999), 257(3), 807-813
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

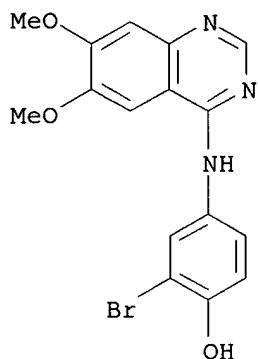
AB We investigated the role of JAK3 in IgE receptor/Fc ϵ RI-mediated mast cell responses. IgE/antigen induced degranulation and mediator release were substantially reduced with Jak3-/- mast cells from JAK3-null mice that were generated by targeted disruption of Jak3 gene in embryonic stem cells. Further, treatment of mast cells with (3'bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154), a potent inhibitor of JAK3, inhibited degranulation and proinflammatory mediator release after IgE receptor/ Fc ϵ RI crosslinking. Thus, JAK3 plays a pivotal role in IgE receptor/ Fc ϵ RI-mediated mast cell responses and targeting JAK3 may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions.
(c) 1999 Academic Press.

IT 211555-04-3, Whi-p154

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic and biochem. evidence for critical role of Janus Kinase (JAK)-3 in mast cell-mediated type I hypersensitivity reactions and inhibition by)

RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 36 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:190747 HCAPLUS

DOCUMENT NUMBER: 131:344

TITLE: Irreversible inhibition of epidermal growth factor receptor tyrosine kinase with in vivo activity by N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-2-butynamide (CL-378,785)

AUTHOR(S): Discafani, Carolyn M.; Carroll, Marion L.; Floyd, M. Brawner, Jr.; Hollander, Irwin J.; Husain, Zaheed; Johnson, Bernard D.; Kitchen, Douglas; May, Michael K.; Malo, Madhu S.; Minnick, Albert A., Jr.; Nilakantan, Ramaswamy; Shen, Ru; Wang, Yu-Fen; Wissner, Allan; Greenberger, Lee M.

CORPORATE SOURCE: Oncology and Immunoinflammatory Research,

Wyeth-Ayerst Research, Pearl River, NY, 10965, USA

SOURCE: Biochemical Pharmacology (1999), 57(8), 917-925

CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It has been shown previously that 4-anilino quinazolines compete with the ability of ATP to bind the epidermal growth factor receptor (EGF-R), inhibit EGF-stimulated autophosphorylation of tyrosine residues in EGF-R, and block EGF-mediated growth. Since millimolar concns. of ATP in cells could reduce the efficacy of 4-anilino quinazolines in cells and the activity of these compds. would not be sustained once they were removed from the body, we reasoned that irreversible inhibitors of EGF-R might improve the activity of this series of compds. in animals. Mol. modeling of the EGF-R kinase domain was used to design irreversible inhibitors. We herein describe one such inhibitor: N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-2-butynamide, known as CL-387,785. This compound covalently bound to EGF-R. It also specifically inhibited kinase activity of the protein (IC₅₀ = 370 ± 120 pM), blocked EGF-stimulated autophosphorylation of the receptor in cells (IC₅₀ ~ 5 nM), inhibited cell proliferation (IC₅₀ = 31-125 nM) primarily in a cytostatic manner in cell lines that overexpress EGF-R or c-erbB-2, and profoundly blocked the growth of a tumor that overexpresses EGF-R in nude mice (when given orally at 80 mg/kg/day for 10 days, daily). We conclude that CL-387,785 is useful for studying the interaction of small mols. with EGF-R and may have clin. utility.

IT 194423-06-8, CL 387785

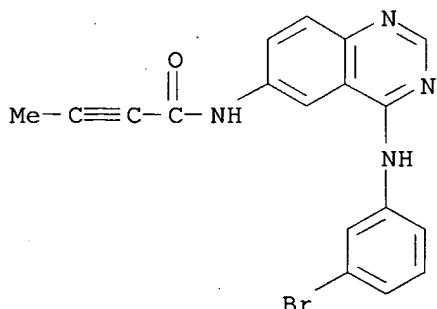
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(irreversible inhibition of epidermal growth factor receptor tyrosine kinase with)

RN 194423-06-8 HCAPLUS

CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 37 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:172597 HCAPLUS

DOCUMENT NUMBER: 130:209716

TITLE: Preparation of 2-vinyl-4-aminoquinazoline derivatives as insulin secretion promoters and antidiabetics

INVENTOR(S): Ueno, Kimihisa; Nomoto, Yuji; Takasaki, Kotaro; Yoshida, Miho; Kusaka, Hideaki; Yano, Hiroshi; Nakanishi, Satoshi; Matsuda, Yuzuru; Uesaka, Noriaki; Suzuki, Chiharu

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; et al.

SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|------------|-----------------|------------|
| WO 9909986 | A1 | 19990304 | WO 1998-JP3711 | 19980821 |
| W: AU, BG, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9887487 | A | 19990316 | AU 1998-87487 | 19980821 |
| PRIORITY APPLN. INFO.: | | | JP 1997-225963 | A 19970822 |
| | | | WO 1998-JP3711 | W 19980821 |
| OTHER SOURCE(S): GI | MARPAT | 130:209716 | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Claimed are insulin secretion promoters and remedies for diabetes which

contain as the active ingredient 2-vinyl-4-aminoquinazoline derivs. represented by general formula (I) or pharmacol. acceptable salts thereof [wherein R1A and R1B are the same or different and each represents hydrogen, lower alkyl, lower alkoxy, halogeno, nitro, NR₃R₄ (wherein R₃ and R₄ are the same or different and each represents hydrogen or lower alkyl), etc.; or R1A may form together with R1B adjacent thereto O(CH₂)_nO (wherein n is 1 or 2); Cy represents optionally substituted aryl; R₂ represents hydrogen or optionally substituted lower alkyl; and A represents hydrogen or optionally substituted lower alkyl, optionally substituted cycloalkyl, etc.; or R₂ and A may form together with the nitrogen atom adjacent thereto an optionally substituted heterocycle]. These compds. exhibited insulin secretion activity at high concentration of glucose (14.5 mM) but no substantial activity at low concentration of glucose (\leq 5 mM). For comparison, glubenzamide did exhibit substantial insulin-secretion activity at low concentration of glucose. Thus, 7-chloro-7-methoxy-2-[2-(E)-(2,4-dimethoxyphenyl)vinyl]quinazoline was condensed with N-methylphenethylamine to give the title compound (II). II in vitro showed insulin secretion activity of 3,413 ng/mL at 1 μ M under 14.5 mM glucose and 86 ng/mL at 10 μ M under 5 mM glucose in spleen β -cells (MIN6) as compared to that of 684 ng/mL at 0.1 μ M under 14.5 mM glucose and 317 ng/mL at 0.1 μ M under 5 mM glucose for glubenzamide.

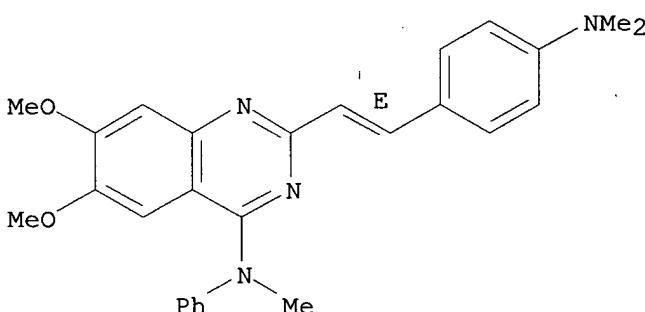
IT 221008-60-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vinylaminoquinazoline derivs. as insulin secretion promoters and antidiabetics)

RN 221008-60-2 HCAPLUS

CN 4-Quinazolinamine, 2-[(1E)-2-[4-(dimethylamino)phenyl]ethenyl]-6,7-dimethoxy-N-methyl-N-phenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 38 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:129333 HCAPLUS

DOCUMENT NUMBER: 130:332267

TITLE: Use of a Pharmacophore Model for the Design of EGFR Tyrosine Kinase Inhibitors: Isoflavones and 3-Phenyl-4(1H)-quinolones

AUTHOR(S): Traxler, Peter; Green, Jennifer; Mett, Helmut; Sequin, Urs; Furet, Pascal

CORPORATE SOURCE: NOVARTIS Pharmaceuticals Therapeutic Area Oncology, NOVARTIS Limited, Basel, CH-4002, Switz.

SOURCE: Journal of Medicinal Chemistry (1999), 42(6),

1018-1026
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

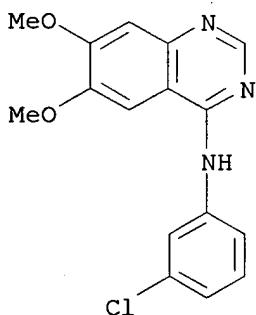
AB Using a pharmacophore model for ATP-competitive inhibitors interacting with the active site of the EGFR protein tyrosine kinase together with published X-ray crystal data of quercetin in complex with the Hck tyrosine kinase and of deschloroflavopiridol in complex with CDK2, a putative binding mode of the isoflavone genistein (I) was proposed. Then, based on literature data suggesting that a salicylic acid function, which is represented by the 5-hydroxy-4-keto motif in I, could serve as a pharmacophore replacement of a pyrimidine ring, superposition of I onto the potent EGFR tyrosine kinase inhibitor 4-(3'-chlorophenylamino)-6,7-dimethoxyquinazoline led to 3'-chloro-5,7-dihydroxyisoflavone (II) as a target structure which in fact was 10 times more potent than I. The putative binding mode of II suggests a sulfur-aromatic interaction of the m-chlorophenyl moiety with Cys 773 in the "sugar pocket" of the EGFR kinase model. Replacement of the oxygen in the chromenone ring of II by a nitrogen atom further improved the inhibitory activity against the EGFR kinase.

IT 153436-53-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (use of a pharmacophore model for design of EGFR tyrosine kinase inhibitors: isoflavones and 3-phenyl-4(IH)-quinolones)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 39 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:77207 HCPLUS
 DOCUMENT NUMBER: 130:209666
 TITLE: A decarboxylative traceless linker approach for the solid phase synthesis of quinazolines
 Cobb, James M.; Fiorini, Maria T.; Goddard, Chris R.; Theoclitou, Maria-Elena; Abell, Chris
 University Chemical Laboratory, Cambridge, CB2 1EW, UK
 Tetrahedron Letters (1999), 40(5), 1045-1048
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

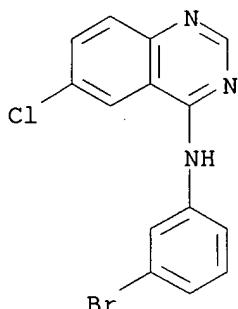
AB A decarboxylative traceless linker strategy for the cleavage of resin-bound quinazolines has been developed using hydroxymethylpolystyrene (HMPS) resin derivatized as the Et oxalate. Methods for the solid phase synthesis of the linker, quinazoline formation, functionalization, and cleavage are described.

IT 220912-95-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(decarboxylative traceless linker approach for the solid phase synthesis of quinazolines)

RN 220912-95-8 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6-chloro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 40 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:63563 HCPLUS

DOCUMENT NUMBER: 130:261387

TITLE: Pharmacokinetics and biologic activity of the novel mast cell inhibitor, 4-(3'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline in mice

AUTHOR(S): Chen, Chun-Lin; Malaviya, Ravi; Navara, Christopher; Chen, Hao; Bechard, Brian; Mitcheltree, Greg; Liu, Xing-Ping; Uckun, Fatih M.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, Hughes Institute, St. Paul, MN, 55113, USA

SOURCE: Pharmaceutical Research (1999), 16(1), 117-122
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of the present study was to examine the pharmacodynamic and pharmacokinetic features of the novel mast cell inhibitor 4-(3'-Hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P180) in mice. A high performance liquid chromatog. (HPLC)-based quant. detection method was used to measure plasma WHI-P-180 levels in mice. The plasma concentration-time data was fit to a single compartment pharmacokinetic model by using the WinNonlin program to calculate the pharmacokinetic parameters. A cutaneous anaphylaxis model was used to examine the pharmacodynamic effects of WHI-P180 on anaphylaxis-associated vascular hyperpermeability. The elimination half-life of WHI-P180 in CD-1 mice (BALB/c mice) following i.v., i.p., or p.o. administration was less than 10 min. Systemic clearance of WHI-P180 was 6742 mL/h/kg in CD-1 mice and 8188 mL/h/kg in BALB/c mice. Notably, WHI-P180, when administered in two consecutive nontoxic i.p. bolus doses of 25 mg/kg, inhibited IgE/antigen-induced vascular hyperpermeability in a well-characterized murine model of passive cutaneous anaphylaxis. WHI-P180 is an active inhibitor of IgE-mediated

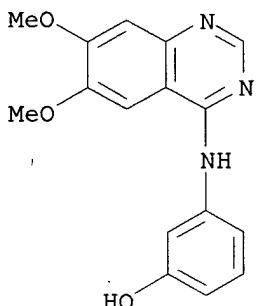
mast cell responses in vitro and in vivo. Further preclin. characterization of WHI-P180 may improve the efficacy of WHI-P180 in vivo and provide the basis for design of effective treatment and prevention programs for mast cell- mediated allergic reactions.

IT 211555-08-7, WHI-P 180

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (mastocyte inhibitor quinazoline derivative WHI-P180 pharmacokinetics and pharmacodynamics)

RN 211555-08-7 HCAPLUS

CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 41 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:711702 HCAPLUS

DOCUMENT NUMBER: 130:63543

TITLE: Antibacterial effect of some 2,6-disubstituted 4-anilinoquinazolines

AUTHOR(S): Göttasova, R.; Kubikova, J.; Cipak, L.

CORPORATE SOURCE: Department of Biochemistry and Microbiology, Faculty of Chemical Technology, Slovak University of Technology, Bratislava, 812 37, Slovakia

SOURCE: Folia Microbiologica (Prague) (1998), 43(6), 679-682

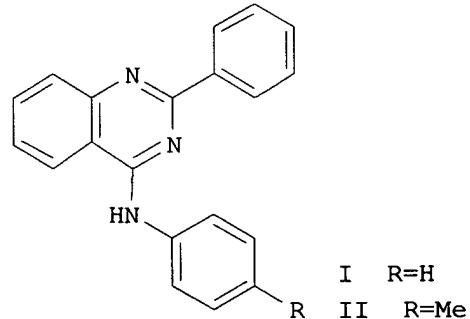
CODEN: FOMIAZ; ISSN: 0015-5632

PUBLISHER: Institute of Microbiology, Academy of Sciences of the Czech Republic

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Two synthetic 2,6-disubstituted 4-anilinoquinazolines (I and II) exerted a significant effect on the Gram-pos. bacteria *Bacillus subtilis* and *Staphylococcus aureus*. None of 12 tested derivs. influenced *Escherichia coli*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*. Derivs. having the aromatic ring non-substituted or substituted by bromine, the pyrimidine ring by Ph, morpholine or piperidine and the aniline skeleton non-substituted or substituted by Me or amino group exerted a considerable antibacterial activity. II is considered as a potential antibacterial compound

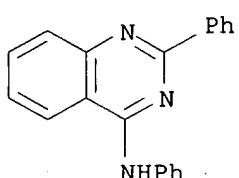
IT 40288-70-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibacterial effect of some disubstituted anilinoquinazolines)

RN 40288-70-8 HCPLUS

CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 42 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:698779 HCPLUS
 DOCUMENT NUMBER: 130:104886
 TITLE: Inhibition of human glioblastoma cell adhesion and invasion by 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154)
 AUTHOR(S): Narla, Rama Krishna; Liu, Xing-Ping; Klis, Daniel; Uckun, Fatih M.
 CORPORATE SOURCE: Drug Discovery Program, Department of Experimental Oncology, Wayne Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Clinical Cancer Research (1998), 4(10), 2463-2471
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Glioblastoma multiforme is a highly invasive primary brain tumor with a disappointingly high local recurrence rate and mortality despite intensive multimodality treatment programs. Therefore, new agents that are capable of inhibiting the infiltration of normal brain parenchyma by glioblastoma cells are urgently needed. Here, we show that the novel quinazoline derivs. 4-(4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) are potent inhibitors of glioblastoma cell adhesion and migration. Specifically, both compds. inhibited at micromolar concns.: (a) integrin-mediated glioblastoma cell adhesion to the extracellular matrix proteins laminin, type IV collagen, and fibronectin; (b) integrin-independent epidermal growth factor-induced adhesion of glioblastoma cells to poly-L-lysine-coated tissue culture plates; (c) fetal bovine serum-induced polymerization of actin and actin stress fiber

formation as well epidermal growth factor-stimulated formation of focal adhesion plaques in serum-starved glioblastoma cells; and most importantly, (d) glioblastoma cell migration in in vitro assays of tumor cell invasiveness using tumor cell spheroids and/or Matrigel-coated Boyden chambers. Further preclin. development of WHI-P131 and WHI-P154 may provide the basis for the design of more effective adjuvant chemotherapy programs for glioblastoma multiforme..

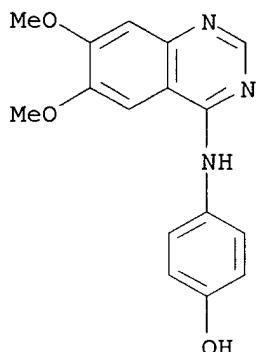
IT 202475-60-3, WHI-P 131

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines WHI-P131 and WHI-P154)

RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

45

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 43 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:649256 HCAPLUS

DOCUMENT NUMBER: 130:10391

TITLE: Specific, irreversible inactivation of the epidermal growth factor receptor and erbB2, by a new class of tyrosine kinase inhibitor

AUTHOR(S): Fry, David W.; Bridges, Alexander J.; Denny, William A.; Doherty, Annette; Greis, Kenneth D.; Hicks, James L.; Hook, Kenneth E.; Keller, Paul R.; Leopold, Wilbur R.; Loo, Joseph A.; McNamara, Dennis J.; Nelson, James M.; Sherwood, Veronika; Smaill, Jeff B.; Trumpp-Kallmeyer, Susanne; Dobrusin, Ellen M.

CORPORATE SOURCE: Department of Cancer Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48106, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(20), 12022-12027

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A class of high-affinity inhibitors is disclosed that selectively target and irreversibly inactivate the epidermal growth factor receptor tyrosine kinase through specific, covalent modification of a cysteine residue present in the ATP binding pocket. A series of expts. employing MS, mol. modeling, site-directed mutagenesis, and 14C-labeling studies in viable cells unequivocally demonstrate that these compds. selectively bind to the

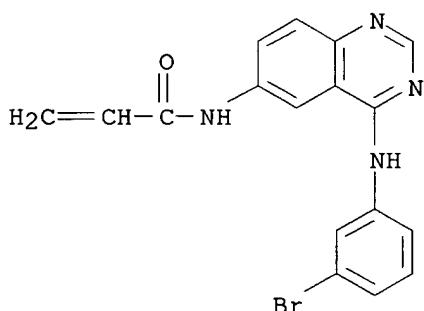
catalytic domain of the epidermal growth factor receptor with a 1:1 stoichiometry and alkylate Cys-773. While the compds. are essentially non-reactive in solution, they are subject to rapid nucleophilic attack by this particular amino acid when bound in the ATP pocket. The mol. orientation and positioning of the acrylamide group in these inhibitors in relation to Cys-773 entirely support these results as determined from docking expts. in a homol.-built mol. model of the ATP site. Evidence is also presented to indicate that the compds. interact in an analogous fashion with erbB2 but have no activity against the other receptor tyrosine kinases or intracellular tyrosine kinases that were tested in this study. Finally, a direct comparison between 6-acrylamido-4-anilinoquinazoline and an equally potent but reversible analog shows that the irreversible inhibitor has far superior in vivo antitumor activity in a human epidermoid carcinoma xenograft model with no overt toxicity at therapeutically active doses. The activity profile for this compound is prototypical of a generation of tyrosine kinase inhibitors with great promise for therapeutic significance in the treatment of proliferative disease.

IT 194423-15-9, PD 168393

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (inactivation of the epidermal growth factor receptor and erbB2 by a tyrosine kinase inhibitor)

RN 194423-15-9 HCPLUS

CN 2-Propenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 44 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:583555 HCPLUS

DOCUMENT NUMBER: 129:288260

TITLE: Opposing effects of cyclosporin A and tyrphostin AG-1478 indicate a role for Src protein in the cellular control of mineralization

AUTHOR(S): Stekelenburg, Jaqueline; Klein, Benjamin Y.; Ben-Bassat, Hannah; Rojansky, Nathan

CORPORATE SOURCE: Laboratory of Experimental Surgery, Hadassah Medical Center, Jerusalem, Israel

SOURCE: Journal of Cellular Biochemistry (1998), 71(1), 116-126

PUBLISHER: CODEN: JCEBD5; ISSN: 0730-2312
Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

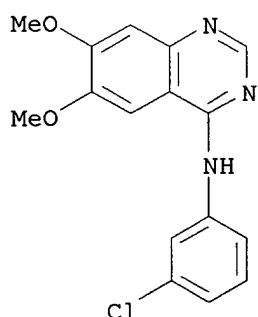
AB Cyclosporin A (CsA) induces osteoporosis but not through direct activation of osteoclasts. CsA also inhibits cell-mediated mineralization in marrow stromal cell culture, whereas the tyrphostin AG-1478 increases mineralization. These antagonistic effects on mineralization were used to discern mols. that underwent phosphorylation changes in association with their opposing effects on mineralization. In parallel, quant. changes in Src protein were followed. Multiple dexamethasone (DEX)-stimulated stromal cell cultures were grown with and without a mineralization-inhibiting dose (0.1 μ M) of CsA and were harvested on different days of DEX stimulation. Immunoblots of gel-fractionated cell exts. showed that the most noticeable changes in tyrosine phosphorylated proteins (TPP) were seen on day 8 of DEX stimulation. At least 15 TPP bands, mostly smaller than 53 kDa, were more prominent in CsA-treated cultures on day 8. Under CsA, Src protein quantity decreased on day 8, but its cleavage product (52/54 kDa) was sixfold more abundant than on day 7. Day 8 was chosen to test the effect of AG-1478 on the CsA-induced TPP changes. DMSO (DMSO) alone, the solvent of AG-1478, increased mineralization in CsA-treated vs. CsA-untreated cultures and slightly decreased Src and its cleavage product. AG-1478 at 5 μ M, in CsA cultures increased the specific alkaline phosphatase activity threefold, with a slight change in mineralization relative to controls grown with DMSO alone. This was accompanied by decreased intensity of several TPP bands smaller than 36 kDa. In contrast, treatment with 50 μ M of AG-1478 increased the intensity of TPP bands at the same mol. size range. This high AG-1478 dose decreased cell counts selecting mineralizing cells. The results indicate that increased Src protein cleavage product on day 8 by CsA is associated with mineralization inhibition, which is opposed by DMSO and 50- μ M AG-1478, thus antagonizing the effect of CsA on mineralization. Direct or indirect interaction between Src and TPP, antagonistically affected by CsA and AG-1478, is likely to underlay cellular control of mineralization. Changes in p19 and p29 intensity showed association with mineralization that was reflected by a significant direct and inverse correlation, resp., with calcium precipitation per cell.

IT 153436-53-4, AG-1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opposing effects of cyclosporin A and tyrphostin AG-1478 indicate a role for Src protein in cellular control of mineralization)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

19

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

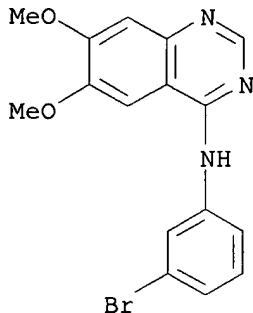
L6 ANSWER 45 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:506709 HCPLUS

DOCUMENT NUMBER: 129:254491
TITLE: EGFR blockade by tyrosine kinase inhibitor or monoclonal antibody inhibits growth, directs terminal differentiation and induces apoptosis in the human squamous cell carcinoma HN5
AUTHOR(S): Modjtahedi, Helmout; Affleck, Karen; Stubberfield, Colin; Dean, Christopher
CORPORATE SOURCE: McElwain Laboratories, The Institute of Cancer Research, Surrey, SG1 2NY, UK
SOURCE: International Journal of Oncology (1998), 13(2), 335-342
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human squamous cell carcinomas frequently overexpress the epidermal growth factor receptor (EGFR) and this is often associated with poor prognosis in patients with these cancers. The high level of expression of the EGFR provides an important target for therapy and we and others have shown that monoclonal antibodies (mAbs) which block the activation of the receptor by the EGF family of ligands inhibit the growth of EGFR overexpressing tumors in vitro and induce the regression of established tumors grown as xenografts in athymic mice. Inhibitors of the tyrosine kinase associated with the EGFR have also been shown to block receptor activation and prevent tumor cell proliferation. Using the EGFR-overexpressing head and neck carcinoma cell line HN5, we have compared the biol. consequences of treatment with an inhibitor of EGFR tyrosine kinase (PD153035) with anti-EGFR monoclonal antibodies (mAbs) ICR63 or ICR80. We found that both the anti-EGFR mAbs and the TK inhibitor produce similar biol. changes namely, they inhibit the EGF and TGF α -induced tyrosine phosphorylation of the receptor and the growth in culture of HN5 cells. At concns. above 100 nM, the TK inhibitor prevented the growth in culture of HN5 cells completely with an IC50 of 40 nM. With the anti-EGFR mAbs, growth of HN5 cells was inhibited completely at concns. above 4 nM with an IC50 of 1 nM. More importantly we found that, like the anti-EGFR mAbs, treatment with the TK inhibitor directs HN5 cells to undergo terminal differentiation as monitored by the expression of cytokeratin 10. In addition, our results indicate that the growth inhibitory effects of the anti-EGFR agents also lead to induction of apoptosis as determined by 7-amino actinomycin D staining (7-AAD). We conclude that EGFR blockade by anti-EGFR mAbs or TK inhibitor influences the growth in culture of EGFR overexpressing tumors by directing terminal differentiation and inducing apoptosis.

IT 153436-54-5, PD153035
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EGFR blockade by tyrosine kinase inhibitor or monoclonal antibody inhibits growth, directs terminal differentiation and induces apoptosis in the human squamous cell carcinoma HN5)

RN 153436-54-5 HCAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 46 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:505889 HCPLUS
 Correction of: 1996:73866
 DOCUMENT NUMBER: 129:109067
 Correction of: 124:232395
 TITLE: Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor
 AUTHOR(S): Newcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.
 CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, 92019, N. Z.
 SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-928
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC₅₀ 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC₅₀ of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC₅₀ 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding

competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC₅₀ 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC₅₀ of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC₅₀s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

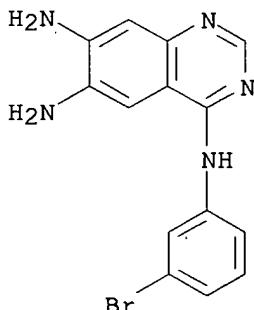
IT 169205-87-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)

RN 169205-87-2 HCPLUS

CN 4,6,7-Quinazolinetriamine, N4-(3-bromophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 47 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:500993 HCPLUS

DOCUMENT NUMBER: 129:140790

TITLE: The use of LC-API/MS with photodiode array detection for the determination of impurities in drug synthesis

Taylor, Steve; Preece, Steve

AUTHOR(S): Structure-Purity Group, Zeneca Pharmaceuticals,
CORPORATE SOURCE: Alderley Park, Macclesfield, Cheshire, SK10 4TG, UKSOURCE: American Biotechnology Laboratory (1998), 16(8), 29-30
CODEN: ABLAEY; ISSN: 0749-3223

PUBLISHER: International Scientific Communications, Inc.

DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Peaks in the eluate from liquid chromatog. of synthetic quinazoline derivative I

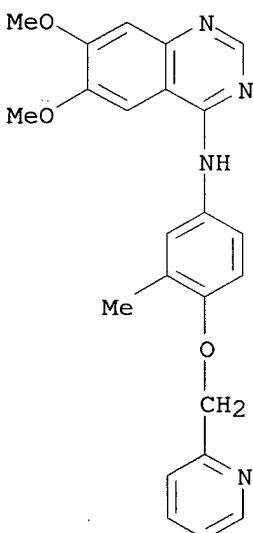
were subjected to atmospheric pressure ionization mass spectrometry (API/MS) at low and high cone voltages and to photodiode array detection (DAD) over a scan range of 190-600 nm. A faster-eluting impurity in I was detected at a level of 6.9% and identified as 4-chloro-6,7-dimethoxyquinazoline by the above methods. API/MS and DAD complement one another, since compds. that are not readily ionized may be detected by DAD, and impurities that do not contain a strong chromophore may be detected by ionization and fragmentation with MS.

IT 179688-83-6

RL: ANT (Analyte); ANST (Analytical study)
 (the use of LC-API/MS with photodiode array detection for determination of impurities in drug synthesis)

RN 179688-83-6 HCPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-[3-methyl-4-(2-pyridinylmethoxy)phenyl]-(9CI) (CA INDEX NAME)



L6 ANSWER 48 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:492839 HCPLUS

DOCUMENT NUMBER: 129:213579

TITLE: Role of tyrosine kinases in induction of the c-jun proto-oncogene in irradiated B-lineage lymphoid cells

AUTHOR(S): Goodman, Patricia A.; Niehoff, Lisa B.; Uckun, Fatih M.

CORPORATE SOURCE: Department of Molecular Genetics, Wayne Hughes Institute, St. Paul, MN, 55113, USA

SOURCE: Journal of Biological Chemistry (1998), 273(28), 17742-17748

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Exposure of B-lineage lymphoid cells to ionizing radiation induces an elevation of c-jun proto-oncogene mRNA levels. This signal is abrogated

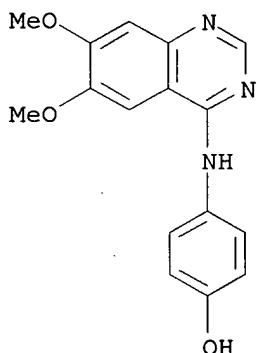
by protein-tyrosine kinase (PTK) inhibitors, indicating that activation of an as yet unidentified PTK is mandatory for radiation-induced c-jun expression. Here, we provide exptl. evidence that the cytoplasmic tyrosine kinases BTK, SYK, and LYN are not required for this signal. Lymphoma B-cells rendered deficient for LYN, SYK, or both by targeted gene disruption showed increased c-jun expression levels after radiation exposure, but the magnitude of the stimulation was lower than in wild-type cells. Thus, these PTKs may participate in the generation of an optimal signal. Notably, an inhibitor of JAK-3 (Janus family kinase-3) abrogated radiation-induced c-jun activation, prompting the hypothesis that a chicken homolog of JAK-3 may play a key role in initiation of the radiation-induced c-jun signal in B-lineage lymphoid cells.

IT 202475-60-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (role of tyrosine kinases in induction of c-jun proto-oncogene in irradiated B-lineage lymphoid cells)

RN 202475-60-3 HCPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

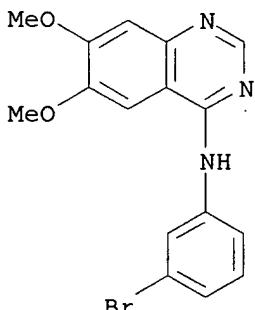
L6 ANSWER 49 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:486591 HCPLUS
 DOCUMENT NUMBER: 129:202915
 TITLE: Synthesis of [methoxy-11C]PD153035, a selective EGF receptor tyrosine kinase inhibitor
 AUTHOR(S): Johnstrom, Peter; Fredriksson, Anna; Thorell, Jan-Olov; Stone-Elander, Sharon
 CORPORATE SOURCE: Karolinska Pharmacy, Stockholm, S-171 76, Swed.
 SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1998), 41(7), 623-629
 CODEN: JLCRD4; ISSN: 0362-4803
 PUBLISHER: John Wiley & Sons Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB [Methoxy-11C]PD153035, a potent and specific inhibitor of the EGF receptor tyrosine kinase, was prepared by O-alkylation of O-desmethyl PD153035 with [11C]methyl iodide in DMF. The radiochem. incorporation of [11C]CH₃I was on the order of 45%. The mean specific activity obtained at end-of-synthesis was 26 GBq/ μ mol (n=3; range 20-36 GBq/ μ mol) and total synthesis time was 45-50 min including formulation.
 IT 153436-54-5P, PD153035

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of [methoxy-11C]PD153035)

RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 50 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:465544 HCPLUS

DOCUMENT NUMBER: 129:239536

TITLE: Inhibition of growth of primary human tumor cell cultures by a 4-anilinoquinazoline inhibitor of the epidermal growth factor receptor family of tyrosine kinases

AUTHOR(S): Baguley, B. C.; Marshall, E. S.; Holdaway, K. M.; Newcastle, G. W.; Denny, W. A.

CORPORATE SOURCE: Cancer Research Laboratory, University of Auckland School of Medicine, Auckland, N. Z.

SOURCE: European Journal of Cancer (1998), 34(7), 1086-1090
CODEN: EJCAEL; ISSN: 0959-8049

PUBLISHER: Elsevier Science Ltd.

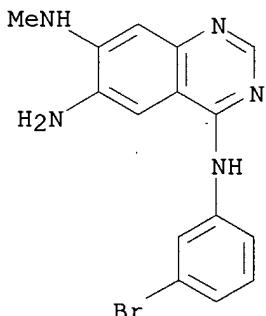
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The epidermal growth factor receptor (EGFR) is thought to mediate the action of the mitogens EGF and tumor growth factor- α (TGF- α) in a variety of cancers, including those of the lung, breast and ovary. A number of new selective inhibitors of EGFR tyrosine kinase have now been developed as potential new antitumor agents. We used a potent inhibitor of this tyrosine kinase, 6-amino-4-[(3-bromophenyl)amino]-7-(methylamino)quinazoline (SN 25531; PD 156273), to determine the responses of primary cultures derived from patients with cancer of the lung, ovary, breast, cervix and endometrium. Cells were cultured in 96-well plates and proliferation assessed by incorporation of 3H-thymidine. Measured growth inhibitory concns. IC50 values varied from 1 nM to 14 μ M with a 1000-fold differential between sensitive and resistant cultures. Results were compared with rates of proliferation, estimated using a paclitaxel-based method. We also measured the IC50 values for the tyrosine kinase inhibitor using a number of established human cell lines, and compared them with EGFR content using fluorescent antibody staining and flow cytometry. The presence of EGFR was necessary, but not sufficient, for in vitro response. Only a small number of cell lines (3 of 7 for lung, 1 of 7 for ovarian, 2 of 3 squamous cell and 0 of 12 for melanoma) were sensitive to the tyrosine kinase inhibitor. In contrast, 40 of the 50 primary cultures (including 14 of 15 lung cancer samples and 14 of 19 ovarian cancer samples) were sensitive.

10/ 715,773

IT 171745-04-3, PD 156273
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of growth of primary human tumor cell cultures by a 4-anilinoquinazoline inhibitor of the epidermal growth factor receptor family of tyrosine kinases)
RN 171745-04-3 HCAPLUS
CN 4,6,7-Quinazolinetriamine, N4-(3-bromophenyl)-N7-methyl- (9CI) (CA INDEX NAME)

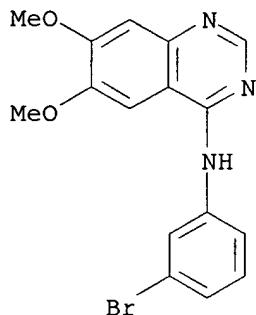


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 51 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:411534 HCAPLUS
DOCUMENT NUMBER: 129:148959
TITLE: The title research P. Traxler, et al. (1997) is reviewed with commentary and 20 refs.
AUTHOR(S): Trumpp-Kallmeyer, Susanne; Showalter, H. D. Hollis
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division Warner-Lambert Company, Ann Arbor, MI, USA
SOURCE: Chemtracts (1998), 11(7), 550-560
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title research of P. Traxler, et al. (1997) is reviewed with commentary and 20 refs.
IT 153436-54-5, PD 153035
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of pharmacophore model for design of epidermal growth factor receptor (EGFr) tyrosine kinase inhibitors, i.e.
(phenylamino)pyrazolo[3,4-d]pyrimidines)
RN 153436-54-5 HCAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

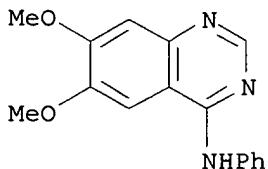
L6 ANSWER 52 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:401227 HCAPLUS
 DOCUMENT NUMBER: 129:170172
 TITLE: 4-(3'-Bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline: a novel quinazoline derivative with potent cytotoxic activity against human glioblastoma cells
 AUTHOR(S): Narla, Rama Krishna; Liu, Xing-Ping; Myers, Dorothea E.; Uckun, Fatih M.
 CORPORATE SOURCE: Department of Experimental Oncology, Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Clinical Cancer Research (1998), 4(6), 1405-1414
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The novel quinazoline derivative 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) exhibited significant cytotoxicity against U373 and U87 human glioblastoma cell lines, causing apoptotic cell death at micromolar concns. The in vitro antiglioblastoma activity of WHI-P154 was amplified >200-fold and rendered selective by conjugation to recombinant human epidermal growth factor (EGF). The EGF-P154 conjugate was able to bind to and enter target glioblastoma cells within 10-30 min via receptor (R)-mediated endocytosis by inducing internalization of the EGF-R mols. In vitro treatment with EGF-P154 resulted in killing of glioblastoma cells at nanomolar concns. with an IC₅₀ of 813 ± 139 nM, whereas no cytotoxicity against EGF-R-neg. leukemia cells was observed, even at concns. as high as 100 μM. The in vivo administration of EGF-P154 resulted in delayed tumor progression and improved tumor-free survival in a severe combined immunodeficient mouse glioblastoma xenograft model. Whereas none of the control mice remained alive tumor-free beyond 33 days (median tumor-free survival, 19 days) and all control mice had tumors that rapidly progressed to reach an average size of >500 mm³ by 58 days, 40% of mice treated for 10 consecutive days with 1 mg/kg/day EGF-P154 remained alive and free of detectable tumors for more than 58 days with a median tumor-free survival of 40 days. The tumors developing in the remaining 60% of the mice never reached a size >50 mm³. Thus, targeting WHI-P154 to the EGF-R may be useful in the treatment of glioblastoma multiforme.

IT 21561-09-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glioblastoma inhibition by quinazoline derivative WHI-P154 targeting of EGF receptor)

RN 21561-09-1 HCAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



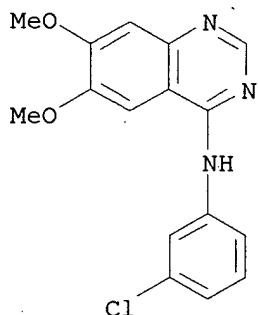
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 53 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:400243 HCPLUS
 DOCUMENT NUMBER: 129:156456
 TITLE: Inhibition of Cdk2 activation by selected tyrphostins causes cell cycle arrest at late G1 and S phase
 AUTHOR(S): Kleinberger-Doron, Nurit; Shelah, Noa; Capone, Ricardo; Gazit, Aviv; Levitzki, Alexander
 CORPORATE SOURCE: Department of Biological Chemistry, Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, 91904, Israel
 SOURCE: Experimental Cell Research (1998), 241(2), 340-351
 CODEN: ECREAL; ISSN: 0014-4827
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The authors have previously reported that certain tyrphostins which block EGF-R phosphorylation in cell-free systems fail to do so in intact cells. Nevertheless, the authors found that this family of tyrphostins inhibits both EGF- and calf serum-induced cell growth and DNA synthesis [Osherov, N.A., Gazit, C., Gilon, and Levitzki, A. (1993). Selective inhibition of the EGF and HER2/Neu receptors by Tyrphostins. J. Biol. Chemical 268, 11134-11142.]; now the authors show that these tyrphostins exert their inhibitory activity even when added at a time when the cells have already passed their restriction point and receptor activation is no longer necessary. AG555 and AG556 arrest 85% of the cells at late G1, whereas AG490 and AG494 cause cells to arrest at late G1 and during S phase. No arrest occurs during G2 or M phase. Further anal. revealed that these tyrphostins act by inhibiting the activation of the enzyme Cdk2 without affecting its levels or its intrinsic kinase activity. Furthermore, they do not alter the association of Cdk2 to cyclin E or cyclin A or to the inhibitory proteins p21 and p27. These compds. also have no effect on the activating phosphorylation of Cdk2 by Cdk2 activating kinase (CAK) and no effect on the catalytic domain of cdc25 phosphatase. These compds. lead to the accumulation of phosphorylated Cdk2 on tyrosine 15 which is most probably the cause for its inhibition leading to cell cycle arrest at G1/S. A structure-activity relation study defines a very precise pharmacophore, suggesting a unique mol. target not yet identified and which is most probably involved in the regulation of the tyrosine-phosphorylated state of Cdk2. These compds. represent a new class of cell proliferation blockers whose target is Cdk2 activation. (c) 1998 Academic Press.

IT 153436-53-4, AG1478
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (Inhibition of Cdk2 activation by selected tyrphostins causes cell cycle arrest at late G1 and S phase in relation to tyrosine phosphorylation and structure)

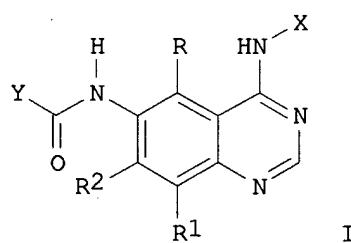
RN 153436-53-4 HCPLUS
 CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 54 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:366894 HCPLUS
 DOCUMENT NUMBER: 129:54379
 TITLE: Preparation of 4-aminoquinazolines as EGFR inhibitors
 INVENTOR(S): Wissner, Allan; Johnson, Bernard D.; Floyd, Middleton B., Jr.; Kitchen, Douglas B.
 PATENT ASSIGNEE(S): American Cyanamid Co., USA
 SOURCE: U.S., 17 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|-----------|-----------------|----------|
| US 5760041 | A | 19980602 | US 1997-785910 | 19970121 |
| PRIORITY APPLN. INFO.: | | | US 1997-785910 | 19970121 |
| OTHER SOURCE(S): | MARPAT | 129:54379 | | |
| GI | | | | |



AB The title compds. [I; X = (un)substituted Ph; R, R1 = H, halo, alkyl, etc.; R2 = H, alkyl, alkoxy, etc.; Y = R3C.tplbond.C, R3C(R3)C:C(R3), etc. (wherein R3 = H, alkyl, carboxy, etc.)] or their pharmaceutically acceptable salts, useful in treating, inhibiting the growth of, or eradicating breast, kidney, bladder, mouth, larynx, esophagus, stomach, colon, ovary and lung neoplasms, were prepared. Thus, reaction of N-(3-bromophenyl)-4,6-quinazolindiamine with 3,3-dimethylacryloyl chloride

in the presence of pyridine in ether afforded I [X = 3-BrC₆H₄; Y = Me₂C:CH; R, R₁, R₂ = H] which showed IC₅₀ of 0.5 μM against EGF receptor kinase.

IT 194423-13-7P

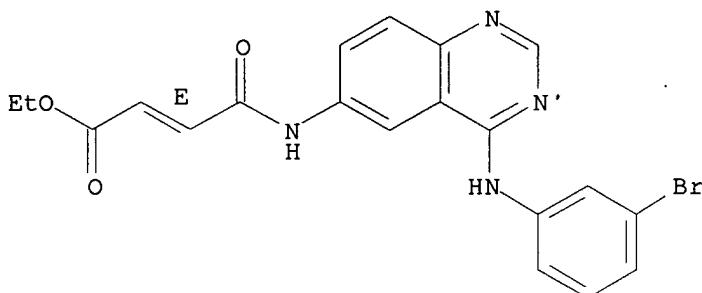
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 4-aminoquinazolines as EGFR inhibitors)

RN 194423-13-7 HCPLUS

CN 2-Butenoic acid, 4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 55 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:323483 HCPLUS

DOCUMENT NUMBER: 129:119500

TITLE: Inhibitors of the epidermal growth factor receptor protein tyrosine kinase. A quantitative structure-activity relationship analysis

AUTHOR(S): Singh, P.; Kumar, R.

CORPORATE SOURCE: Department Chemistry, S. K. Government College, Sikar, 332001, India

SOURCE: Journal of Enzyme Inhibition (1998), 13(2), 125-134
CODEN: ENINEG; ISSN: 8755-5093

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hansch and Free-Wilson analyses are described on a data set, 4-anilinoquinazolines [the analogs of 4-(3-bromo-anilino)-6,7-dimethoxy quinazoline: PD 153035], as inhibitors of the epidermal growth factor receptor protein tyrosine kinase. These analyses have helped to ascertain the role of different substituents in explaining the observed inhibitory activities. From both approaches, it is concluded that the combined electron-donating nature of R₁- and R₂-substitutions of the quinazoline ring and the electron-withdrawing nature of the X-substitution of the anilino-ring are beneficial for increasing the inhibition activity of a compound. Further, the sym. alkoxy substituents present at the R₁- and R₂-positions are also engaged in a steric interaction which was determined quant. through the parabolic relationship between the activity and combined molar refraction parameter, ΣMR of the substituents.

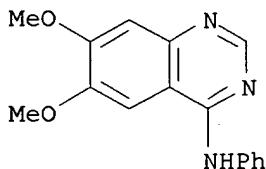
IT 21561-09-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(quant. structure-activity relationship of inhibitors of the epidermal growth factor receptor protein tyrosine kinase)

RN 21561-09-1 HCAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 56 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:319418 HCAPLUS

DOCUMENT NUMBER: 129:62930

TITLE: Inhibition of platelet-derived growth factor and epidermal growth factor receptor signaling events after treatment of cells with specific synthetic inhibitors of tyrosine kinase phosphorylation

AUTHOR(S): Lipson, Kenneth E.; Pang, Long; Huber, L. Julie; Chen, Hui; Tsai, Jian-Ming; Hirth, Peter; Gazit, Aviv; Levitzki, Alexander; McMahon, Gerald

CORPORATE SOURCE: SUGEN, Inc., Redwood City, CA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(2), 844-852

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The receptor kinase activity associated with the epidermal growth factor (EGF) receptor and platelet-derived growth factor (PDGF) receptor plays an important role in ligand-induced signaling events. The effect of specific, synthetic chemical inhibitors of PDGF- and EGF-mediated receptor tyrosine autophosphorylation on receptor signaling were examined in NIH 3T3 cells overexpressing PDGF or EGF receptors. Specific inhibition of ligand-dependent receptor autophosphorylation, PI3K activation, mitogen-activated protein kinase (MAPK) activation, cyclin E-associated kinase activity and cell proliferation was measured after treatment of cells with these inhibitors. A synthetic PDGF receptor kinase inhibitor exhibited specific inhibitory properties when tested for PDGF-induced receptor autophosphorylation, MAPK activity, PI3K activation, entry into S phase and cyclin E-associated kinase activity. A synthetic EGF receptor kinase inhibitor showed selective inhibitory properties when tested for EGF-induced receptor autophosphorylation, MAPK activation, PI3K activation, entry into S phase and cyclin E-associated kinase activity. In both cases, these compds. were found to be effective as inducers of growth arrest and accumulation of cells in the G1 phase of the cell cycle after ligand treatment. However, at high concns., the EGF receptor kinase inhibitor was observed to exhibit some non-specific effects as demonstrated by attenuation of PDGF-induced receptor autophosphorylation and cell cycle progression. This demonstrates that it is critical to use the lowest concentration

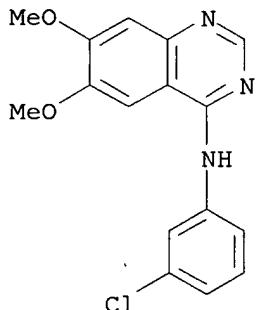
of such an inhibitor that will alter the response under investigation, to have confidence that the conclusions derived from the use of such inhibitor are valid. We conclude that these exptl. parameters signify useful end points to measure the relative selectivity of tyrosine kinase inhibitors that affect receptor-mediated signal transduction.

IT 153436-53-4, AG1478

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (inhibition of platelet-derived growth factor and epidermal growth factor receptor signaling events after treatment of cells with specific synthetic inhibitors of tyrosine kinase phosphorylation)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 57 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:300008 HCPLUS

DOCUMENT NUMBER: 129:90001

TITLE: Inhibition of epidermal growth factor receptor kinase induces protease-dependent apoptosis in human colon cancer cells

AUTHOR(S): Karnes, William E., Jr.; Weller, Shaun G.; Adjei, Philip N.; Kottke, Timothy J.; Glenn, Kahil S.; Gores, Gregory J.; Kaufmann, Scott H.

CORPORATE SOURCE: Division of Gastroenterology, Mayo Clinic, Rochester, MN, USA

SOURCE: Gastroenterology (1998), 114(5), 930-939
 CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The epidermal growth factor receptor (EGFR) is under investigation as a therapeutic target for cancers. Colon cancer cell lines are variably dependent on autocrine stimulation of EGFR. We therefore examined the effects of a selective EGFR tyrosine kinase inhibitor, PD 153035, on proliferation and survival of five colon cancer cell lines whose autonomous proliferation is either EGFR ligand dependent or EGFR ligand independent. Effects of inhibitors were screened by MTS growth assays, [³H]thymidine incorporation, terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling assay, fluorescence microscopy, immunoblotting, and in vitro protease assays. PD 153035 caused dose-dependent cytostasis (200 nmol/L to 1 µmol/L) and apoptosis (>10 µmol/L) in ligand-dependent cell lines and caused variable apoptosis (>10 µmol/L) but no cytostasis in ligand-independent cell lines. Apoptosis induced by 10 µmol/L PD 153035 was not associated with induction of p53 protein expression but was accompanied by activation of caspases that cleave poly(ADP-ribose) polymerase, lamin B1, and Bcl-2. Inhibition of caspase 3-like protease activity by DEVD-fluoromethylketone significantly delayed the onset of PD 153035-induced apoptosis. The EGFR tyrosine kinase inhibitor PD 153035 induces cytostasis and

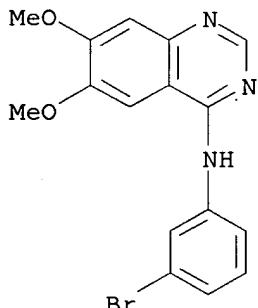
caspase-dependent apoptosis in EGFR ligand-dependent colon cancer cell lines. These observations encourage further investigation of EGFR tyrosine kinase inhibitors for treatment of colorectal neoplasms.

IT 153436-54-5, PD 153035

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(protease-dependent apoptosis in human colon cancer cells induced by inhibition of epidermal growth factor receptor kinase)

RN 153436-54-5 HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 58 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:282401 HCAPLUS

DOCUMENT NUMBER: 128:321653

TITLE: Preparation of alkynyl- and azido-substituted 4-anilinoquinazolines for the treatment of hyperproliferative diseases

INVENTOR(S): Schnur, Rodney Caughren; Arnold, Lee Daniel

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S., 23 pp.

DOCUMENT TYPE: CODEN: USXXAM

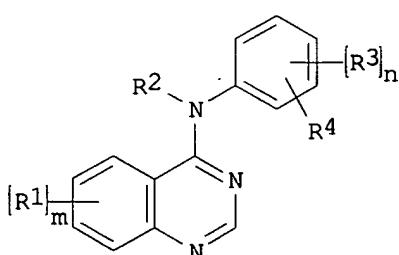
LANGUAGE: Patent

FAMILY ACC. NUM. COUNT: English

PATENT INFORMATION: 1

PRIORITY APPLN. INFO.: OTHER SOURCE(S): GI

| PATENT NO., ----- | KIND ----- | DATE ----- | APPLICATION NO. ----- | DATE ----- |
|-------------------|------------|------------|--|----------------------|
| US 5747498 | A | 19980505 | US 1996-653786
US 1996-653786 | 19960528
19960528 |
| PRIORITIES: | | | CASREACT 128:321653; MARPAT 128:321653 | |



I

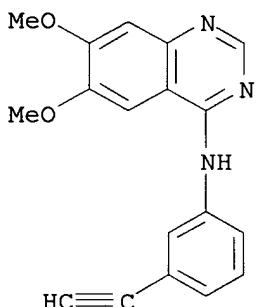
AB The title compds. [I; R1 = H, halo, OH, etc.; R2 = H, (un)substituted C1-6 alkyl; R3 = H, halo, OH, etc.; R4 = N3, (un)substituted ethynyl; m = 1-3; n = 1-2] and their salts, useful in the treatment of hyperproliferative diseases such as cancer, were prepared. Thus, reaction of 4-chloro-6,7-dimethoxyquinazoline with 4-azidoaniline hydrochloride in iPrOH afforded 98% I [R1 = 6,7-Me₂; R2, R3 = H; R4 = 4-N3]. Compds. I showed IC₅₀ of 0.0001-30 μM against EGFR kinase.

IT 183319-26-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alkynyl- and azido-substituted 4-anilinoquinazolines for the treatment of hyperproliferative diseases)

RN 183319-26-8 HCPLUS

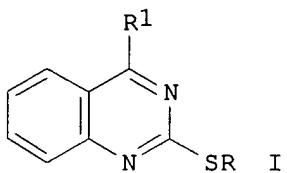
CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 59 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:266137 HCPLUS
 DOCUMENT NUMBER: 128:321611
 TITLE: Tautomerism and reactivity of substituted pyrimidines.
 60 Synthesis of 2-alkyl(benzyl)thio-4-aryl(heteroaryl,
 benzyl)aminoquinazolines
 AUTHOR(S): Abdullaev, N. P.; Kayumov, K.; Shakhidoyatov, Kh. M.
 CORPORATE SOURCE: Inst. Khim. Rastit. Veshchestv, AN RUz, Uzbekistan
 SOURCE: Uzbekskii Khimicheskii Zhurnal (1997), (2), 29-33
 CODEN: UZKZAC; ISSN: 0042-1707
 PUBLISHER: Fan
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI



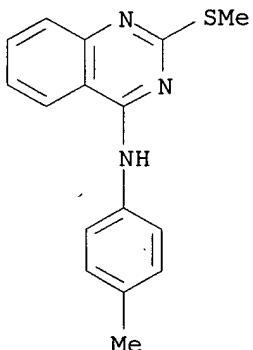
AB Title compds. such as I (R = C1-C4 n-alkyl, benzyl; R1 = NHPh, NHCH₂Ph, piperidino, morpholino) were prepared by reaction of I (same R; R1 = Cl) with amines. Yields were usually ≥90%.

IT 207127-40-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 207127-40-0 HCPLUS

CN 4-Quinazolinamine, N-(4-methylphenyl)-2-(methylthio)-, monohydrochloride
(9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 60 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:180763 HCPLUS

DOCUMENT NUMBER: 128:261949

TITLE: Use of quinazoline derivatives for the manufacture of a medicament in the treatment of hyperproliferative skin disorders

INVENTOR(S): McMahon, Gerald; Shawver, Laura Kay; Narog, Blair; Tang, Peng Cho; Hirth, Klaus Peter

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

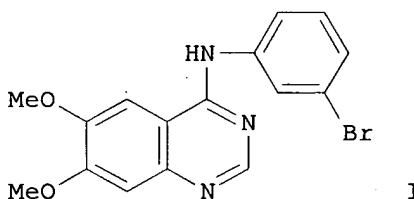
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| WO 9810767 | A2 | 19980319 | WO 1997-US16145 | 19970911 |
| WO 9810767 | A3 | 19980806 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
 VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
 GN, ML, MR, NE, SN, TD, TG
 CA 2265630 A1 19980319 CA 1997-2265630 19970911
 AU 9743429 A 19980402 AU 1997-43429 19970911
 EP 954315 A2 19991110 EP 1997-941542 19970911
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 US 6004967 A 19991221 US 1997-927442 19970911
 PRIORITY APPLN. INFO.:
 US 1996-26067P P 19960913
 US 1996-31436P P 19961120
 US 1997-34981P P 19970108
 US 1997-48372P P 19970603
 WO 1997-US16145 W 19970911

OTHER SOURCE(S): MARPAT 128:261949

GI



AB Quinazolines, e.g. I, useful for treating hyperproliferative skin disorders, are prepared. Thus, Me 2-amino-4,5-dimethoxybenzoate was cyclocondensed with formamidine acetate to give 6,7-dimethoxy-4-quinazolone, which was chlorinated with thionyl chloride to give the 4-chloro compound. The latter compound was aminated with 3-bromoaniline to give I-HCl, which was converted to the free base. The quinazolines inhibit epidermal growth factor (EGF) receptor phosphorylation as well as EGF-mediated skin cell growth and psoriatic skin cell proliferation. Specifically, I potently inhibited ligand-induced autophosphorylation of the EGF receptor, and downstream signal transduction events, including DNA replication and cell cycle progression. I was specific for the EGF receptor. Radiolabeled I penetrated human cadaver skin, reaching biol. effective concs. in the epidermis within a 24-h period. A topical formulation contains I 1.0, mineral oil 5.00, glyceryl monostearate 3.00, benzyl alc. 0.75, oleic acid 2.50, butylated hydroxytoluene 0.001 and white petrolatum qs to 100%.

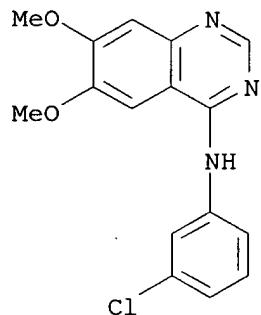
IT 153436-53-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

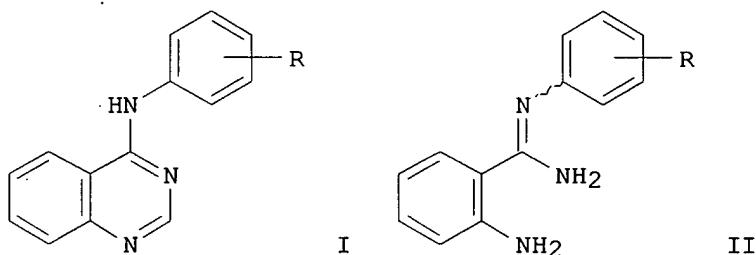
(preparation of quinazolines for the treatment of hyperproliferative skin disorders)

RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 61 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:176913 HCAPLUS
 DOCUMENT NUMBER: 128:244010
 TITLE: Synthesis of 4-arylaminoquinazolines via
 2-amino-N-arylbenzamidines
 AUTHOR(S): Szczepankiewicz, Wojciech; Suwinski, Jerzy
 CORPORATE SOURCE: Institute of Organic Chemistry and Technology,
 Silesian Technical University, Gliwice, 44-100, Pol.
 SOURCE: Tetrahedron Letters (1998), 39(13), 1785-1786
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 128:244010
 GI



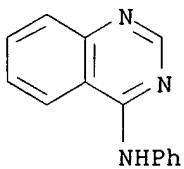
AB A new synthesis of twelve 4-arylaminoquinazolines, I ($R = H, 3\text{-Br}, 3,4\text{-Me}_2$, etc.), from 2-amino-N-arylbenzamidines II and formic acid is described. The entering amidines were obtained in the reaction of anthranilonitrile with 50% molar excess of aromatic amines and anhydrous aluminum chloride.

IT 34923-95-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of arylaminoquinazolines from arylaminobenzamidines)

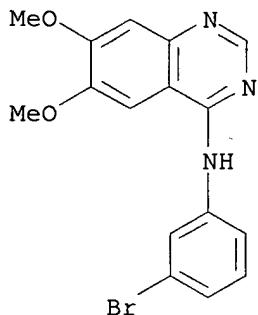
RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



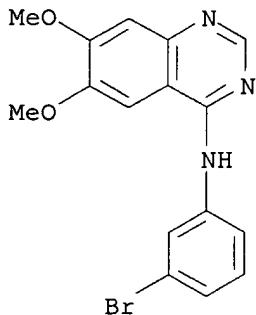
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 62 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:39812 HCPLUS
 DOCUMENT NUMBER: 128:175891
 TITLE: A specific inhibitor of the epidermal growth factor receptor tyrosine kinase
 AUTHOR(S): Fry, David W.; Kraker, Alan J.; McMichael, Amy; Ambroso, Linda A.; Nelson, James M.; Leopold, Wilbur R.; Connors, Richard W.; Bridges, Alexander J.
 CORPORATE SOURCE: Parke-Davis Pharm. Res., Div. of Warner-Lambert Co., Ann Arbor, MI, 48105, USA
 SOURCE: Science (Washington, D. C.) (1994), 265(5175), 1093-1095
 CODEN: SCIEAS; ISSN: 0036-8075
 PUBLISHER: American Association for the Advancement of Science
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A small mol. called PD 153035 inhibited the epidermal growth factor (EGF) receptor tyrosine kinase with a 5-pM inhibition constant. The inhibitor was specific for the EGF receptor tyrosine kinase and inhibited other purified tyrosine kinases only at micromolar or higher concns. PD 153035 rapidly suppressed autophosphorylation of the EGF receptor at low nanomolar concns. in fibroblasts or in human epidermoid carcinoma cells and selectively blocked EGF-mediated cellular processes including mitogenesis, early gene expression, and oncogenic transformation. PD 153035 demonstrates an increase in potency over that of other tyrosine kinase inhibitors of four to five orders of magnitude for inhibition of isolated EGF receptor tyrosine kinase and three to four orders of magnitude for inhibition of cellular phosphorylation.
 IT 153436-54-5, PD 153035
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (A specific inhibitor of the epidermal growth factor receptor tyrosine kinase)
 RN 153436-54-5 HCPLUS
 CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

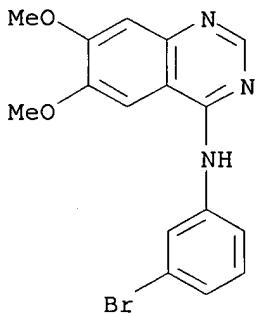
L6 ANSWER 63 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:20167 HCPLUS
 DOCUMENT NUMBER: 128:162549
 TITLE: A novel series of 4-phenoxyquinolines: potent and highly selective inhibitors of PDGF receptor autophosphorylation
 AUTHOR(S): Kubo, Kazuo; Shimizu, Toshiyuki; Ohyama, Shin-Ichi; Murooka, Hideko; Nishitoba, Tsuyoshi; Kato, Shinichiro; Kobayashi, Yoshiko; Yagi, Mikio; Isoe, Toshiyuki; Nakamura, Kazuhide; Osawa, Tatsushi; Izawa, Toshio
 CORPORATE SOURCE: Pharmaceutical Research Laboratory, KIRIN Brewery Co., Ltd., Takasaki, 370-12, Japan
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(23), 2935-2940
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A novel series of 4-phenoxyquinolines, some of which showed potent and highly selective inhibitory activities for PDGF receptor autophosphorylation, was discovered. Interestingly, their structures were very similar to those of the selective inhibitors for EGF receptor autophosphorylation.
 IT 153436-54-5, PD153035
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (4-phenoxyquinolines as potent and highly selective inhibitors of PDGF receptor autophosphorylation)
 RN 153436-54-5 HCPLUS
 CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 64 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:767348 HCPLUS
 DOCUMENT NUMBER: 128:70482
 TITLE: PD153035, a tyrosine kinase inhibitor, prevents epidermal growth factor receptor activation and inhibits growth of cancer cells in a receptor number-dependent manner
 AUTHOR(S): Bos, Monique; Mendelsohn, John; Kim, Young-Mee; Albanell, Joan; Fry, David W.; Baselga, Jose
 CORPORATE SOURCE: Laboratory of Receptor Biology and Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
 SOURCE: Clinical Cancer Research (1997), 3(11), 2099-2106
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB PD153035 is reported to be a specific and potent inhibitor of the epidermal growth factor (EGF) receptor tyrosine kinase and, to a lesser degree, of the closely related HER2/neu receptor. We show that PD153035 inhibits EGF-dependent EGF receptor phosphorylation and suppresses the proliferation and clonogenicity of a wide panel of EGF receptor-overexpressing human cancer cell lines. EGF receptor autophosphorylation in response to exogenous EGF was completely inhibited at PD153035 concns. of >75 nM in cells overexpressing the EGF receptor. In contrast, PD153035 only reduced heregulin-dependent tyrosine phosphorylation in HER2/neu-overexpressing cell lines at significantly higher concns. (1400-2800 nM). PD153035 exposure did not affect the expression of either EGF receptors or HER2/neu. PD153035 caused a dose-dependent growth inhibition of EGF receptor-overexpressing cell lines at low micromolar concns., and the IC₅₀ in monolayer cultures was less than 1 μM in most cell lines tested. At doses of up to 2.5 μM, the IC₅₀ for HER2/neu-overexpressing cells was not reached. In colony-forming assays, the PD153035 growth-inhibitory activity in cultures driven by endogenous (autocrine) ligand was correlated with EGF receptor number, with higher activity in cells expressing higher nos. of EGF receptors and only minimal activity in cells expressing normal nos. of EGF receptors but high HER2/neu levels. PD153035 also abolished all growth effects mediated by the addition of exogenous EGF; this condition could be reversed upon removal of the compound. Cotreatment with C225, and anti-EGF receptor-blocking monoclonal antibody, further enhanced the antitumor activity of PD153035, suggesting mechanisms of action for C225 other than competition with ligand binding. This latter finding also suggests that combined anti-EGF receptor strategies may be of enhanced benefit against tumors with high

levels of EGF receptor expression.
 IT 153436-54-5, PD153035
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tyrosine kinase inhibitor PD153035 prevents epidermal growth factor receptor activation and inhibits cancer growth)
 RN 153436-54-5 HCPLUS
 CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 65 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:729400 HCPLUS
 DOCUMENT NUMBER: 128:43513
 TITLE: Induction of apoptosis and cell cycle arrest by CP-358774, an inhibitor of epidermal growth factor receptor tyrosine kinase
 AUTHOR(S): Moyer, James D.; Barbacci, Elsa G.; Iwata, Kenneth K.; Arnold, Lee; Boman, Bruce; Cunningham, Ann; Diorio, Catherine; Doty, Jonathan; Morin, Michael J.; Moyer, Mikal P.; Neveu, Mark; Pollack, Vincent A.; Pustilnik, Leslie R.; Reynolds, Margaret M.; Sloan, Don; Theleman, April; Miller, Penny
 CORPORATE SOURCE: Pfizer Central Research, Groton, CT, 06340, USA
 SOURCE: Cancer Research (1997), 57(21), 4838-4848
 CODEN: CNREA8; ISSN: 0008-5472
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The epidermal growth factor receptor (EGFR) is overexpressed in a significant percentage of carcinomas and contributes to the malignant phenotype. CP-358774 is a directly acting inhibitor of human EGFR tyrosine kinase with an IC₅₀ of 2 nM and reduces EGFR autophosphorylation in intact tumor cells with an IC₅₀ of 20 nM. This inhibition is selective for EGFR tyrosine kinase relative to other tyrosine kinases we have examined, both in assays of isolated kinases and whole cells. At doses of 100 mg/kg, CP-358774 completely prevents EGF-induced autophosphorylation of EGFR in human HN5 tumors growing as xenografts in athymic mice and of the hepatic EGFR of the treated mice. CP-358774 inhibits the proliferation of DiFi human colon tumor cells at submicromolar concns. in cell culture and blocks cell cycle progression at the G1 phase. This inhibitor produces a marked accumulation of retinoblastoma protein in its underphosphorylated form and accumulation of p27KIP1 in DiFi cells, which may contribute to the cell cycle block. Inhibition of the EGFR also triggers apoptosis in these cells as determined by formation of DNA fragments

and other criteria. These results indicate that CP-358774 has potential for the treatment of tumors that are dependent on the EGFR pathway for proliferation or survival.

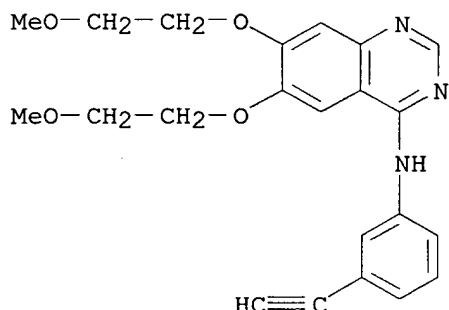
IT 183319-69-9, CP 358774

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(EGF receptor inhibitor CP-358774 induction of apoptosis and cell cycle arrest)

RN 183319-69-9 HCPLUS

CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 66 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:712093 HCPLUS

DOCUMENT NUMBER: 128:13236

TITLE: v-Triazolines. Part 38. New synthesis of 4-aminoquinazolines and 6-aminopurines

AUTHOR(S): Erba, Emanuela; Sporchia, Daniela

CORPORATE SOURCE: Istituto Chimica Organica, Facolta Farmacia, Univ. degli Studi Milano, Milan, I-20133, Italy

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1997), (20), 3021-3024

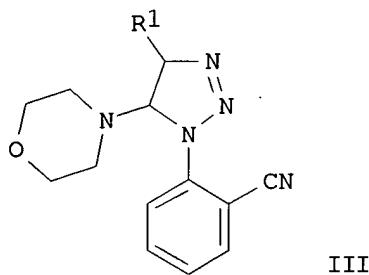
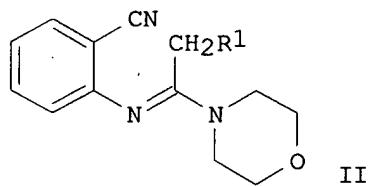
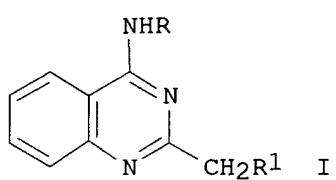
PUBLISHER: CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Royal Society of Chemistry

LANGUAGE: Journal

OTHER SOURCE(S): English

GI: CASREACT 128:13236



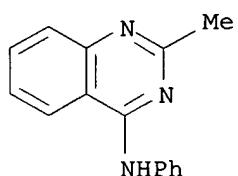
AB 2-Alkyl-4-arylaminoquinazolines I [R = C₆H₄OEt-4, C₆H₄OMe-4, C₆H₄Cl-4, C₆H₄OMe-3, C₆H₄F-3, R₁ = Et; R = Me, CH₂Ph, R₁ = Ph] have been prepared by condensation of N-(2-cyanophenyl)amidines II with arylamines. II were obtained by thermal rearrangement of N-(2-cyanophenyl)-5-morpholino-v-triazolines III. The synthesis has also been applied to the preparation of some 2-alkyl-6-arylaminoquinoxalines.

IT 57942-18-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 4-aminoquinazolines and 6-aminopurines via triazolines)

RN 57942-18-4 HCAPLUS

CN 4-Quinazolinamine, 2-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 67 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:705327 HCAPLUS

DOCUMENT NUMBER: 128:177

TITLE: Identification of epidermal growth factor receptor and c-erbB2 pathway inhibitors by correlation with gene expression patterns

AUTHOR(S): Wosikowski, Katja; Schuurhuis, Danita; Johnson, Kathryn; Paull, Kenneth D.; Myers, Timothy G.; Weinstein, John N.; Bates, Susan E.

CORPORATE SOURCE: Division of Clinical Sciences, Medicine Branch, National Cancer Institute, Bethesda, MD, USA

SOURCE: Journal of the National Cancer Institute (1997), 89(20), 1505-1515

PUBLISHER: CODEN: JNCIEQ; ISSN: 0027-8874
Oxford University Press

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Growth factor receptor-signaling pathways are potentially important targets for anticancer therapy. The interaction of anticancer agents with specific mol. targets can be identified by correlating target expression patterns with cytotoxicity patterns. The authors sought to identify new agents that target and inhibit the activity of the epidermal growth factor (EGF) receptor and of c-erbB2 (also called HER2 or neu), by correlating EGF receptor, transforming growth factor (TGF)- α (a ligand for EGF receptor), and c-erbB2 mRNA expression levels with the results of cytotoxicity assays of the 49 000 compds. in the National Cancer Institute (NCI) drug screen database. The levels of mRNAs were measured and used to generate a mol. target database for the 60 cell lines of the NCI anticancer drug screen. The computer anal. program, COMPARE, was used to search for cytotoxicity patterns in the NCI drug screen database that were highly correlated with EGF receptor, TGF- α , or c-erbB2 mRNA expression patterns. The putative EGF receptor-inhibiting compds. were tested for effects on basal tyrosine phosphorylation, in vitro EGF receptor tyrosine kinase activity, and EGF-dependent growth. Putative ErbB2-inhibiting compds. were tested for effects on antibody-induced ErbB2 tyrosine kinase activity. EGF receptor mRNA and TGF- α mRNA levels were highest in cell lines derived from renal cancers, and c-erbB2 mRNA levels were highest in cells derived from breast, ovarian, and colon cancers. Twenty-five compds. with high correlation coeffs. (for cytotoxicity and levels of the measured mRNAs) were tested as inhibitors of the EGF receptor or c-erbB2 signaling pathways; 14 compds. were identified as inhibitors of these pathways. The most potent compound, B4, inhibited autophosphorylation (which occurs following activation) of ErbB2 by 50% in whole cells at 7.7 μ M. Novel EGF receptor or c-erbB2 pathway inhibitors can be identified in the NCI drug screen by correlation of cytotoxicity patterns with EGF receptor or c-erbB2 mRNA expression levels.

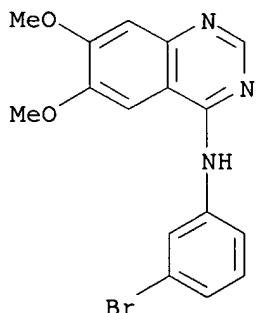
IT 153436-54-5, PD153035

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(identification of epidermal growth factor receptor and c-erbB2 signaling pathway inhibitors by correlation with gene expression patterns and anticancer cytotoxicity using computer program COMPARE)

RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 68 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:644519 HCPLUS

DOCUMENT NUMBER: 127:293185

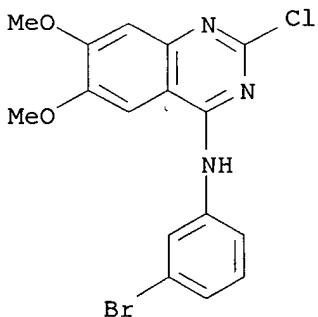
TITLE: A short and unequivocal synthesis of 5-aminotetrazolo[1,5-a]quinazoline as a tricyclic

analog of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline
(PD 153035)

AUTHOR(S): Bencteux, Edith; Houssin, Raymond; Henichart, Jean-Pierre
CORPORATE SOURCE: Institut de Chimie Pharmaceutique, Universite de Lille 2, Lille, 59006, Fr.
SOURCE: Journal of Heterocyclic Chemistry (1997), 34(4), 1375-1378
CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The discovery of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor led to the preparation of several fused tricyclic quinazoline analogs. The present paper reports a new tricyclic derivative: 5-(3-bromoanilino)-7,8-dimethoxytetrazolo[1,5-a]quinazoline. This compound was synthesized by two different pathways via a 1,3-dipolar cycloaddn. of an azide at carbon 2 of the quinazoline ring.

IT 197231-36-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminotetrazoloquinazoline as PD 153035 analog)
RN 197231-36-0 HCPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-2-chloro-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 69 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:621104 HCPLUS
DOCUMENT NUMBER: 127:303614
TITLE: Unliganded epidermal growth factor receptor dimerization induced by direct interaction of quinazolines with the ATP binding site
AUTHOR(S): Arteaga, Carlos L.; Ramsey, Timothy T.; Shawver, Laura K.; Guyer, Cheryl A.
CORPORATE SOURCE: Departments of Medicine and Cell Biology, Vanderbilt Cancer Center and the Department of Veteran Affairs Medical Center, Vanderbilt University School of Medicine, Nashville, TN, 37232-5536, USA
SOURCE: Journal of Biological Chemistry (1997), 272(37), 23247-23254
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Receptor dimerization is critical for signaling by the epidermal growth factor receptor (EGFR) tyrosine kinase. This occurs after binding of the receptor's extracellular domain by ligand or bivalent antibodies. The role of other receptor domains in dimerization is less clear, and there are no examples of dimers induced by direct perturbation of the EGFR kinase domain. Submicromolar concns. of AG-1478 and AG-1517, quinazolines specific for inhibition of the EGFR kinase, induced reversible receptor dimerization in vitro and in intact A431 cells. Consistent with the inhibitory effect of quinazolines on receptor kinase activity, the dimers formed lacked a detectable Tyr(P) signal. Quinazoline-induced EGFR dimerization was abrogated in vitro by ATP and the ATP analog adenylyl-5'-yl imidodiphosphate. Receptors with a single-point mutation in the ATP binding site as well as wild-type EGFR with a covalent modification of the ATP site failed to dimerize in response to AG-1478 and AG-1517. These data suggest that EGFR dimerization can be induced by the interaction of quinazolines at the ATP site in the absence of receptor ligand binding. In SKBR-3 cells, the quinazolines induced the formation of inactive EGFR/ErbB-2 heterodimers, potentially sequestering ErbB-2 from interacting with other coreceptors of the ErbB family. Structural studies of the quinazoline interaction with the EGFR tyrosine kinase domain should allow for an anal. of receptor-specific chemical features required for binding to the ATP site and disruption of signaling, a strategy that can be perhaps applied to other tumor cell receptor systems.

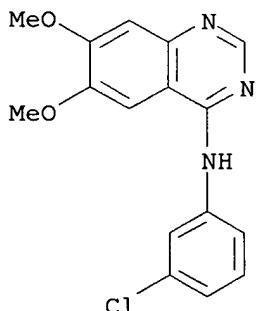
IT 153436-53-4, AG 1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(EGF receptor dimerization induction by quinazoline interaction with ATP binding site)

RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 70 OF 319 HCAPLUS, COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:593456 HCAPLUS

DOCUMENT NUMBER: 127:272367

TITLE: Inhibitors of epidermal growth factor receptor kinase and of cyclin-dependent kinase 2 activation induce growth arrest, differentiation, and apoptosis of human papilloma virus 16-immortalized human keratinocytes
 Ben-Bassat, Hannah; Rosenbaum-Mitrani, Stella;
 Hartzstark, Zippora; Shlomai, Zippora;
 Kleinberger-Doron, Nurit; Gazit, Aviv; Plowman,

AUTHOR(S):

Gregory; Levitzki, Rubina; Tsvieli, Rimona; Levitzki, Alexander

CORPORATE SOURCE: Laboratory of Experimental Surgery, Hadassah University Hospital, Jerusalem, IL-Q1120, Israel

SOURCE: Cancer Research (1997), 57(17), 3741-3750

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human papilloma virus 16 (HPV 16) is associated with cervical cancer and is therefore considered a major health risk for women. Immortalization of keratinocytes induced by HPV infection is largely due to the binding of p53 and Rb by the viral oncoproteins E6 and E7, resp., and is driven to a large extent by a transforming growth factor α /amphiregulin epidermal growth factor receptor autocrine loop. In this study, we show that the growth of HPV 16-immortalized human keratinocytes can be blocked by a selective epidermal growth factor receptor kinase inhibitor, AG 1478, and by AG 555, a blocker of cyclin-dependent kinase 2 (Cdk2) activation. AG 1478 induces a massive increase in the Cdk2 protein inhibitors p27 and p21, whereas AG 555 appears to have a different mechanism of action, inhibiting the activation of Cdk2. Growth arrest induced by AG 1478 and AG 555 is accompanied by up to 20% of cells undergoing apoptosis. Following AG 1478 treatment but not AG 555 treatment, up to 50% of cells undergo terminal keratinocyte differentiation as determined by filaggrin expression and by the decline in the expression of cytokeratin 14. The growth-arresting properties of AG 1478 and AG 555 identifies them as possible lead antipapilloma agents.

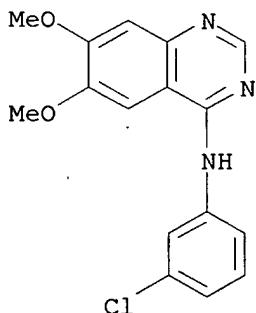
IT 153436-53-4, AG 1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanism of antipapilloma activity of AG 1478 and AG 555)

RN 153436-53-4 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 71 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:520978 HCPLUS

DOCUMENT NUMBER: 127:218645

TITLE: Inhibition of epidermal growth factor receptor gene expression and function decreases proliferation of head and neck squamous carcinoma but not normal mucosal epithelial cells

AUTHOR(S): Grandis, J. Rubin; Chakraborty, A.; Melhem, M. F.;

Zeng, Q.; Twardy, D. J.
CORPORATE SOURCE: Department of Otolaryngology, University of Pittsburgh
and the University of Pittsburgh Cancer Institute,
Pittsburgh, 15213, USA

SOURCE: Oncogene (1997), 15(4), 409-416
CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

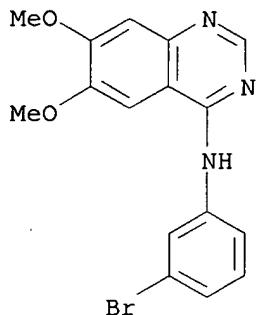
AB Previous reports have shown that fresh tissues and cell lines from patients with squamous cell carcinoma of the head and neck (SCCHN) overexpress transforming growth factor alpha (TGF- α) and its receptor, the epidermal growth factor receptor (EGFR) at both the mRNA and protein levels. Protein localization studies confirm that TGF- α and EGFR are produced by the same epithelial cells in tissues from head and neck cancer patients further supporting an autocrine growth pathway. Using three strategies, the authors examined the hypothesis that down-modulation of EGFR would reduce the proliferation of SCCHN cells. The authors targeted EGFR mRNA using antisense oligonucleotides and the mature EGFR protein at two sites, the ligand-binding domain and the kinase domain, and determined the effects of this targeting on SCCHN proliferation. Treatment of several SCCHN cell lines with a pair of antisense oligodeoxynucleotides directed against the translation start site and first intron-exon splice junction of the human EGFR gene resulted in decreased EGFR protein production and inhibited growth by 86% compared to a 13% reduction in cells treated with sense oligonucleotides. Growth inhibition was specific for carcinoma cells since the same EGFR antisense oligonucleotides had no effect on the proliferation of normal mucosa cells harvested from non-cancer patients. Two monoclonal antibodies which block ligand binding to EGFR (Mabs 425 and 528) inhibited the growth of several SCCHN cell lines by up to 97% which suggests that EGFR is participating in an autocrine pathway in SCCHN i.e., at least in part, external. An EGFR-specific tyrosine kinase inhibitor (PD 153035) was found to inhibit EGFR phosphorylation in SCCHN cell lines and to reduce growth by 68% although it had no effect on the growth rate of normal mucosal epithelial cells. These expts. indicate that EGFR gene expression and function is critical for SCCHN cell growth but not for growth of normal mucosa cells and therefore may serve as a tumor-specific target for preventive and therapeutic strategies in head and neck cancer.

IT 153436-54-5, PD 153035

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of epidermal growth factor receptor gene expression and function decreases proliferation of human head and neck squamous carcinoma but not normal mucosal epithelial cells)

RN 153436-54-5, HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

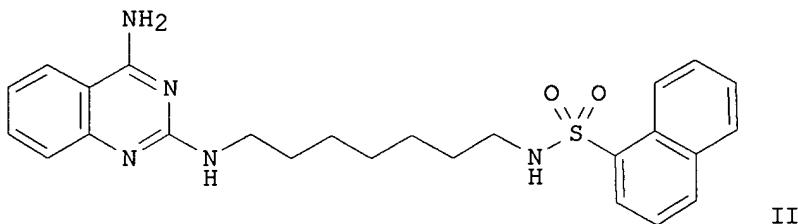
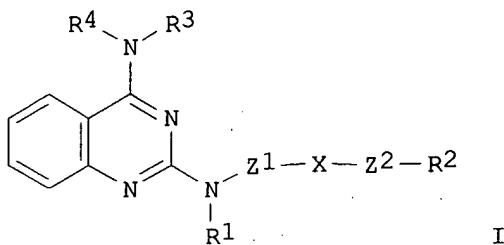


REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 72 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:480974 HCAPLUS
 DOCUMENT NUMBER: 127:95293
 TITLE: Quinazoline derivatives useful as antagonists of NPY receptor subtype Y5
 INVENTOR(S): Rueger, Heinrich; Schmidlin, Tibur; Rigollier, Pascal; Yamaguchi, Yasuchika; Tintelnot-Blomley, Marina; Schilling, Walter; Criscione, Leoluca; Stutz, Stefan Novartis Ag, Switz.; Rueger, Heinrich; Schmidlin, Tibur; Rigollier, Pascal; Yamaguchi, Yasuchika; Tintelnot-Blomley, Marina; Schilling, Walter; Criscione, Leoluca; Stutz, Stefan
 PATENT ASSIGNEE(S):
 SOURCE: PCT Int. Appl., 110 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9720821 | A1 | 19970612 | WO 1996-EP5056 | 19961118 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9676926 | A | 19970627 | AU 1996-76926 | 19961118 |
| ZA 9610021 | A | 19970601 | ZA 1996-10021 | 19961128 |
| PRIORITY APPLN. INFO.: | | | US 1995-566024 | A2 19951201 |
| | | | WO 1996-EP5056 | W 19961118 |

OTHER SOURCE(S): MARPAT 127:95293
 GI



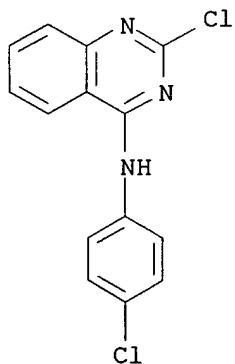
AB The invention relates to a method of treatment of disorders and diseases associated with NPY receptor subtype Y5. The method comprises administration of a therapeutically effective amount of a compound I or a salt thereof [wherein Z1, Z2 = bond, alkylene; R1 = H, alk(en/yn)yl, hydroxyalkyl, cycloalkyl, (hetero)aryl, etc.; R2 = H, halo, NO₂, cyano, alk(en/yn)yl, (un)substituted NH₂, or OH, CO₂H or derivs., etc.; R3, R4 = H, (un)substituted alk(en/yn)yl, aryl, heteroaryl, etc.; or R3R4 = alkylene which may be hetero-atom-interrupted or benzo-fused; X = bond, CH:CH, C.tplbond.C, O, S, SO, SO₂, CO or certain (hemi)ketals; benzo ring of quinazoline nucleus may be substituted]. Also claimed are compds. and pharmaceutical compns. For instance, condensation of 2-chloroquinazolin-4-ylamine with naphthalene-1-sulfonic acid (7-aminoheptyl)amide in isopentyl alc. at 120° gave title compound II, isolated as the HCl salt. In food-deprived rats, II.HCl at 30 mg/kg i.p. gave a 57% inhibition of food intake over 24 h.

IT 174074-90-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazoline derivs. as antagonists of NPY receptor subtype Y5)

RN 174074-90-9 HCPLUS

CN 4-Quinazolinamine, 2-chloro-N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)

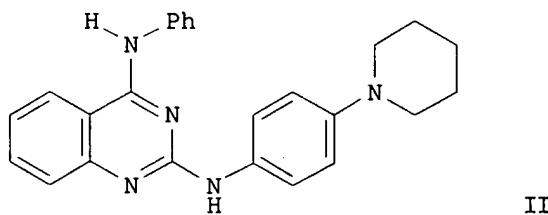
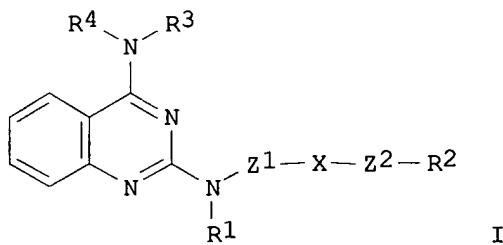


L6 ANSWER 73 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN.
 ACCESSION NUMBER: 1997:480973 HCAPLUS
 DOCUMENT NUMBER: 127:108942
 TITLE: Quinazoline-2,4-diazirines as NPY receptor antagonists
 INVENTOR(S): Rueger, Heinrich; Schmidlin, Tibur; Rigollier, Pascal;
 Yamaguchi, Yasuchika; Tintelnot-Blomley, Marina;
 Schilling, Walter; Criscione, Leoluca
 PATENT ASSIGNEE(S): Novartis Ag, Switz.; Rueger, Heinrich; Schmidlin,
 Tibur; Rigollier, Pascal; Yamaguchi, Yasuchika;
 Tintelnot-Blomley, Marina; Schilling, Walter;
 Criscione, Leoluca
 SOURCE: PCT Int. Appl., 154 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9720822 | A1 | 19970612 | WO 1996-EP5066 | 19961118 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP,
KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG,
SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG | | | | |
| AU 9676928 | A | 19970627 | AU 1996-76928 | 19961118 |
| ZA 9610022 | A | 19970601 | ZA 1996-10022 | 19961128 |
| PRIORITY APPLN. INFO.: | | | US 1995-566027 | A2 19951201 |
| | | | WO 1996-EP5066 | W 19961118 |

OTHER SOURCE(S): MARPAT 127:108942

GI



AB The invention relates to a method of treatment of disorders and diseases associated with NPY receptor subtype Y5. The method comprises administration

of a therapeutically effective amount of a compound I or a salt thereof [wherein Z1, Z2 = bond, alkylene; R1 = H, alk(en/yn)yl, hydroxyalkyl, cycloalkyl, (hetero)aryl, etc.; R2 = H, halo, NO₂, cyano, alk(en/yn)yl, (un)substituted NH₂, or OH, CO₂H or derivs., etc.; R3, R4 = H, (un)substituted alk(en/yn)yl, aryl, heteroaryl, etc.; or R3R4 = alkylene which may be hetero-atom-interrupted or benzo-fused; X = (un)substituted (hetero)arylene; benzo ring of quinazoline nucleus may be substituted]. Also claimed are compds. and pharmaceutical comps. For instance, condensation of 2-chloro-4-(phenylamino)quinazoline with N-(4-aminophenyl)piperidine in a melt gave title compound II, isolated as the HCl salt. In a Y5 receptor binding assay, II.HCl had an IC₅₀ value of 0.01 μM.

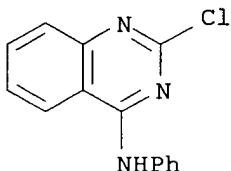
IT 144511-93-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of quinazolinediazirines as antagonists of NPY receptor subtype Y5)

RN 144511-93-3 HCPLUS

CN 4-Quinazolinamine, 2-chloro-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 74 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:480972 HCPLUS

DOCUMENT NUMBER: 127:108941

TITLE: Preparation of 2-aminoquinazolines as neuropeptide Y subtype Y5 receptor antagonists.

INVENTOR(S): Rueger, Heinrich; Schmidlin, Tibur; Rigollier, Pascal; Yamaguchi, Yasuchika; Tintelnot-Bломley, Marina; Schilling, Walter; Criscione, Leoluca; Mah, Robert Novartis Ag, Switz.; Rueger, Heinrich; Schmidlin, Tibur; Rigollier, Pascal; Yamaguchi, Yasuchika; Tintelnot-Bломley, Marina; Schilling, Walter; Criscione, Leoluca; Mah, Robert

PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 166 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9720823 | A2 | 19970612 | WO 1996-EP5067 | 19961118 |
| WO 9720823 | A3 | 19970717 | | |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9676929 | A | 19970627 | AU 1996-76929 | 19961118 |
| ZA 9610020 | A | 19970601 | ZA 1996-10020 | 19961128 |

PRIORITY APPLN. INFO.:

US 1995-566378

A2 19951201

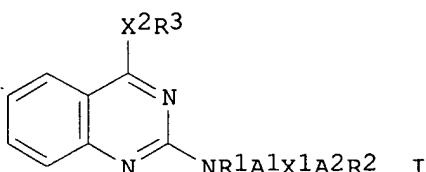
WO 1996-EP5067

W 19961118

OTHER SOURCE(S):

MARPAT 127:108941

GI



AB Title compds. [I; A1, A2 = bond, alkylene; X1, X2 = cycloalkylene, cycloalkenylene, cycloalkylidene, cycloalkenyldene, oxocycloalkylene, oxocycloalkenylene, oxocycloalkylidene, oxocycloalkenyldene; X2 = O, S, SO, SO₂, NR4; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, (hetero)aryl, (hetero)aralkyl; R2 = H, OH, CO₂H, carbamoyl, halo, NO₂, cyano, (substituted) alkyl, amino, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, (hetero)aryl, (hetero)aryalkyl, etc.; R3, R4 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, (hetero)aryl, (hetero)aralkyl; R3R4 = (heteroatom-interrupted) alkylene, (substituted) benzo-fused alkylene], were prepared for treatment of obesity, bulimia nervosa, diabetes, dyslipidemia, hypertension, memory loss, epileptic seizures, migraine, sleep disturbance, pain, sexual/reproductive disorders, depression, anxiety, cerebral hemorrhage, shock, congestive heart failure, nasal congestion, and diarrhea (no data). Thus, 2-chloro-4-phenylaminoquinazoline was heated 4 min. with cyclohexylamine to give 2-cyclohexylamino-4-phenylaminoquinazoline, isolated as the hydrochloride.

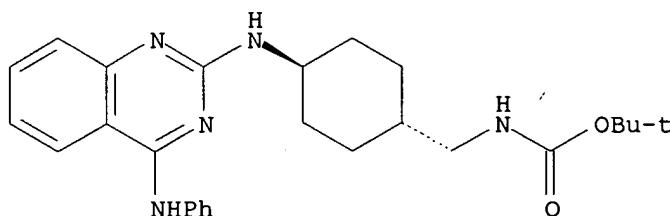
IT 192322-33-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminoquinazolines as neuropeptide Y subtype Y5 receptor antagonists)

RN 192322-33-1 HCPLUS

CN Carbamic acid, [[4-[[4-(phenylamino)-2-quinazolinyl]amino]cyclohexyl]methyl]-, 1,1-dimethylethyl ester, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L6 ANSWER 75 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:296186 HCAPLUS
DOCUMENT NUMBER: 127:757

TITLE: Opposing effects of tyrosine kinase inhibitors on mineralization of normal and tumor bone cells

AUTHOR(S): Klein, B. Y.; Tepper, S.H.; Gal, I.; Shlomai, Z.; Ben-Bassat, H.

CORPORATE SOURCE: Laboratory of Experimental Surgery, Hadassah Medical Center, Jerusalem, 12000, Israel

SOURCE: Journal of Cellular Biochemistry (1997), 65(3), 420-429

CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

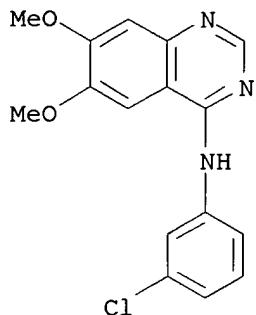
AB Induction of matrix maturation and mineralization in calcified tissues is important for patients with primary bone tumors and other bone deficiencies, e.g., osteoporosis. For the former it signifies a better prognosis in osteosarcoma, and for the latter it might improve bone remodeling. In the present study we exposed osteosarcoma cells (Saos2), normal bone cells, and marrow stroma to two different tyrosine kinase (TK) inhibitors: AG-555 and AG-1478. These tyrphostins differ in their effect on signal transduction downstream to the TK receptor (RTK): AG-1478 inhibits src family TKs whereas AG-555 inhibits nuclear TKs. We found that both tyrphostins at 50 µM increased specific alkaline phosphatase (ALP) activity in Saos2 cells. AG-555 abrogated mineralization whereas AG-1478 increased it. Similarly, in human bone-derived cell cultures the same dose of tyrphostins had an opposing effect on mineralization but, in contrast to AG-555, AG-1478 pos. selected cells with ALP activity. These tyrphostins also differed in their effect on rat marrow stromal cells. AG-555 decreased cell counts unselectively, whereas the decreased cell counts by AG-1478 resulted in selection of osteoprogenitor cells as indicated by a concordant increase in specific ALP activity. The effect of a lower dose of AG-1478, 5 µM, on the increase in mineralization exceeded its own efficiency in selecting cells with specific ALP activity. Our results indicate that AG-1478 selects and preserves the osteoblastic phenotype, at doses moderately higher than those required to induce mineralization, and substantially higher than the doses required for RTK inhibition. Identification of downstream mol. targets for AG-1478, in marrow stromal cells, might prove useful in designing more selective drugs, capable of separating proliferative from differentiation-inducing activities.

IT 153436-53-4, AG 1478

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tyrosine kinase inhibitors opposing effects on mineralization of normal and tumor bone cells)

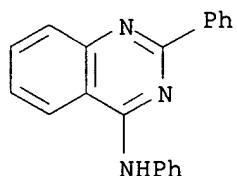
RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

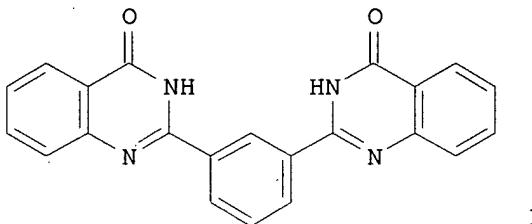


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 76 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:251867 HCPLUS
 DOCUMENT NUMBER: 126:301412
 TITLE: Relationships between the structure, cytotoxicity and hydrophobicity of quinazoline derivatives by quantitative structure-activity relationship.
 AUTHOR(S): Jantova, S.; Balaz, S.; Stankovsky, S.; Spirkova, K.; Lukacova, V.
 CORPORATE SOURCE: Faculty of Chemical Technology, Slovak Technical University, Bratislava, 812 37, Slovakia
 SOURCE: Folia Biologica (Prague) (1997), 43(2), 83-89
 CODEN: FOBLAN; ISSN: 0015-5500
 PUBLISHER: Institute of Molecular Genetics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Cytotoxicities of 93 quinazoline derivs. against HeLa cells were determined as the isoeffective concns. inhibiting, after a single dose, the protein synthesis of 50% of the control amount after 48 h incubation. The dependence of cytotoxicity on hydrophobicity of the studied derivs. has been described using a previously published model-based approach. The studied derivs. are classified into 9 classes each forming a smooth hydrophobicity-cytotoxicity curve. Owing to the acceptable agreement between the model and the data it can be inferred that: (1) the compds. except 2 derivs. bind to the receptors with approx. the same affinity; (2) the criterion for the classification is the different rate of metabolism. The results represent a basis for a rotational development of more potent quinazoline derivs.
 IT 40288-70-8
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (structure-cytotoxicity-hydrophobicity relations of quinazolines)
 RN 40288-70-8 HCPLUS
 CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 77 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:218276 HCAPLUS
 DOCUMENT NUMBER: 126:317357
 TITLE: Synthesis and antimicrobial activity of some
 bis(quinazoline) derivatives
 AUTHOR(S): Shiba, S. A.; El-Khamry, A. A.; Shaban, M. E.; Atia,
 K. S.
 CORPORATE SOURCE: Faculty Science, Ain Shams University, Cairo, Egypt
 SOURCE: Pharmazie (1997), 52(3), 189-194
 CODEN: PHARAT; ISSN: 0031-7144
 PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I

AB Bis[quinazolin-4-on-2-yl]-1,3-phenylene (I) and its 3-N-substituted derivs. were prepared from the corresponding bis[3,1-benzoxazin-4-on-2-yl]-1,3-phenylene as precursor. Quinazolinone I was converted into several derivs. such as bis[quinazolin-4-thioxo-2-yl]-, bis[4-chloroquinazolin-2-yl]-, and bis[4-hydrazinoquinazolin-2-yl]-1,3-phenylene. Some of the prepared compds. show activity against Gram-pos. and Gram-neg. bacteria and yeasts.

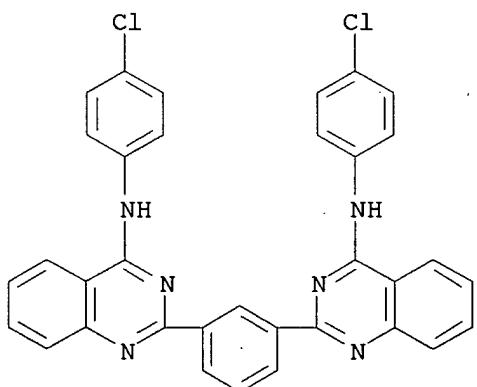
IT 189294-38-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

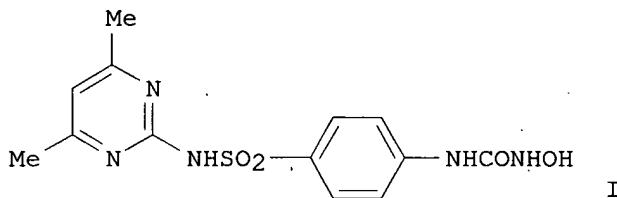
(preparation and antimicrobial activity of bis-quinazolines)

RN 189294-38-0 HCAPLUS

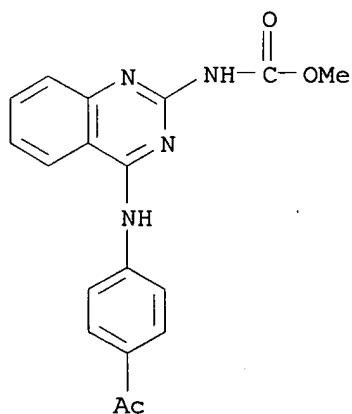
CN 4-Quinazolinamine, 2,2'-(1,3-phenylene)bis[N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 78 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:211735 HCAPLUS
 DOCUMENT NUMBER: 126:251128
 TITLE: Synthesis of hydroxy ureas as inhibitors of 5-lipoxygenase
 AUTHOR(S): Youssef, Khairia M.
 CORPORATE SOURCE: Faculty of Pharmacy, Cairo University, Cairo, Egypt
 SOURCE: Egyptian Journal of Pharmaceutical Sciences (1996), 37(1-6), 531-538
 CODEN: EJPSBZ; ISSN: 0301-5068
 PUBLISHER: National Information and Documentation Centre
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB N-aryl-N'-hydroxyureas, e.g., I, were prepared from arylamines.
 IT 188558-63-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction with hydroxylamine hydrochloride)
 RN 188558-63-6 HCAPLUS
 CN Carbamic acid, [4-[4-acetylphenyl]amino]-2-quinazolinyl-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 79 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:205335 HCAPLUS
 DOCUMENT NUMBER: 126:302017
 TITLE: Specific inhibition of insulin-like growth factor-1 and insulin receptor tyrosine kinase activity and

AUTHOR(S): biological function by tyrphostins
 Parrizas, Marcelina; Gazit, Aviv; Levitzki, Alexander;
 Wertheimer, Efrat; LeRoith, Derek
 CORPORATE SOURCE: National Inst. Diabetes, Digestive and Kidney
 Diseases, NIH, Bethesda, MD, 20892, USA
 SOURCE: Endocrinology (1997), 138(4), 1427-1433
 CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

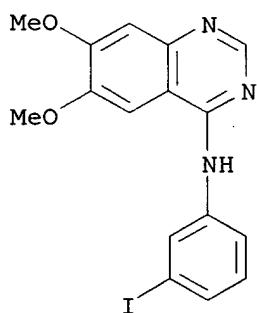
AB A series of the synthetic protein tyrosine kinase inhibitors known as tyrphostins were studied for their effect on insulin-like growth factor-1 and insulin-stimulated cellular proliferation on NIH-3T3 fibroblasts overexpressing either receptor, as well as for their ability to inhibit ligand-stimulated receptor autophosphorylation and tyrosine kinase activity toward exogenous substrates. Several of the tyrphostins tested demonstrated a dramatic effect by inhibiting hormone-stimulated cell proliferation, with IC₅₀s in the submicromolar range, while being unable to block serum-stimulated cell proliferation. The tyrphostins also inhibited receptor autophosphorylation and tyrosine kinase activity, with a higher IC₅₀, in the micromolar range. Most of the tyrphostins tested presented no clear preference for either receptor, although two of them (AG1024 and AG1034) showed significantly lower IC₅₀s for IGF-1 than for insulin receptors. These results suggest that, in spite of the high homol. of the kinase regions of both receptors, it could be possible to design and synthesize small mols. capable of discriminating between them. The synthesis of such specific inhibitors could be an excellent tool to establish the precise signaling mechanisms that distinguish between the different effects of these two hormones.

IT 189290-58-2, AG 1557

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (tyrphostin specific inhibition of IGF-1 and insulin receptor tyrosine kinase activity and biol. function)

RN 189290-58-2 HCPLUS

CN 4-Quinazolinamine, N-(3-iodophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 80 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:173493 HCPLUS
 DOCUMENT NUMBER: 126:233340
 TITLE: Pharmacokinetic-pharmacodynamic analysis of changrolin in dogs with arrhythmia
 AUTHOR(S): Liu, Changxiao; Gu, Yibao; Feng, Jianlin; Wei, Guangli; Xiao, Shuhua; Sun, Jinlin
 CORPORATE SOURCE: Tianjin Institute of Pharmaceutical Research, The State Pharmaceutical Administration, Tianjin, 300193,

SOURCE: Peop. Rep. China
Yaoxue Xuebao (1996), 31(9), 666-670
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Chinese Academy of Medical Sciences, Institute of
Materia Media
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The pharmacokinetics and pharmacodynamics of changrolin (CRL) were studied in 7 dogs with arrhythmia induced by coronary artery ligation. The ECG and the percentage of reduction ratio of ventricular premature beat were used to evaluate the effect of CRL, and a HPLC method was used to determine the serum drug concentration. A pharmacokinetic program was used to fit concentration-time

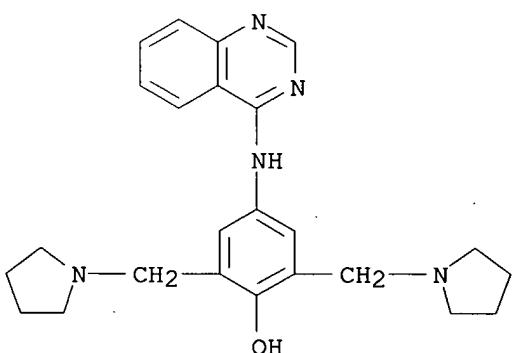
data and a combined pharmacokinetic-pharmacodynamic model was used to analyze effect-time data in the individual dog. After infusion with CRL 83.3 µg/kg-1/min-1 for 60 min, the K10, T1/2, Vd, Cl and Ce were 0.0087 min-1, 78.03 min, 40.55 mL/kg-1, 0.42 mL/kg-1 min-1 and 2.01 µg/mL-1, resp.

IT 72063-47-9, Changrolin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic-pharmacodynamic anal. of changrolin in dogs with arrhythmia)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 81 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:165795 HCPLUS

DOCUMENT NUMBER: 126:264065

TITLE: The synthesis and SAR of new 4-(N-alkyl-N-phenyl)amino-6,7-dimethoxyquinazolines and 4-(N-alkyl-N-phenyl)aminopyrazolo[3,4-d]pyrimidines, inhibitors of CSF-1R tyrosine kinase activity

AUTHOR(S): Myers, Michael R.; Setzer, Natalie N.; Spada, Alfred P.; Persons, Paul E.; Ly, Cuong Q.; Maguire, Martin P.; Zulli, Allison L.; Cheney, Daniel L.; Zilberstein, Asher; Johnson, Susan E.; Franks, Carol F.; Mitchell, Karen J.

CORPORATE SOURCE: Deps. Med. Chem., Rhone-Poulenc Rorer Pharmaceuticals, Collegeville, PA, 19426-0107, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(4), 421-424

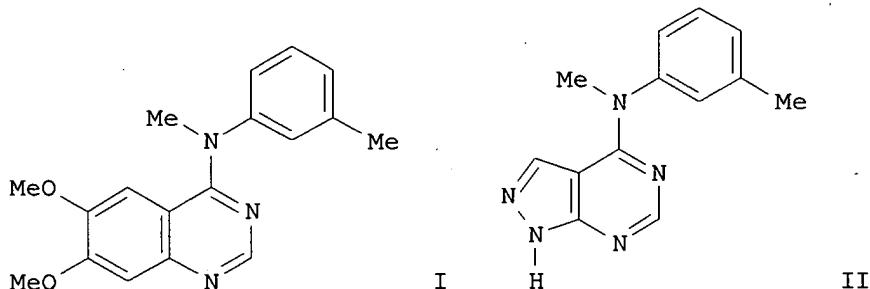
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

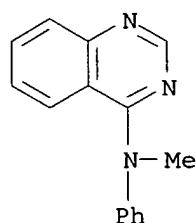
LANGUAGE:
GI

English



AB The authors have identified moderately potent and selective inhibitors of CSF-1R tyrosine kinase activity. A preliminary SAR study resulted in the identification of quinazoline I and pyrazolopyrimidine II as the most potent analogs in the series ($IC_{50} = 0.18 \mu M$). The 3-D-conformation of the 4-(N-alkyl-N-phenyl)-aminoquinazolines has been proposed to be important to the overall selectivity and activity.

IT 74303-57-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (structure activity of pyrazolopyrimidines and quinazolines as CSF-1R tyrosine kinase inhibitors)

RN 74303-57-4 HCPLUS**CN** 4-Quinazolinamine, N-methyl-N-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 82 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:165787 HCPLUS

DOCUMENT NUMBER: 126:264049

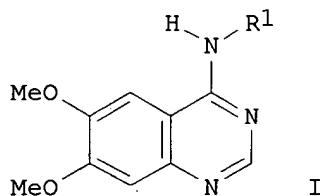
TITLE: The preparation and SAR of 4-(anilino), 4-(phenoxy), and 4-(thiophenoxy)-quinazolines: inhibitors of p56lck and EGF-R tyrosine kinase activity

AUTHOR(S): Myers, Michael R.; Setzer, Natalie N.; Spada, Alfred P.; Zulli, Allison L.; Hsu, Chin-Yi J.; Zilberstein, Asher; Johnson, Susan E.; Hook, Linda E.; Jacoski, Mary V.

CORPORATE SOURCE: Deps. Med. Chem., Rhone-Poulenc Rorer Pharmaceuticals,

SOURCE: Collegeville, PA, 19426-0107, USA
 Bioorganic & Medicinal Chemistry Letters (1997), 7(4),
 417-420
 CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



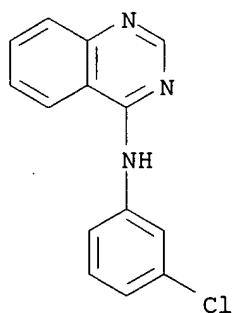
AB The authors report herein their preliminary results of a SAR study of quinazoline-based inhibitors of p51ck and EGF-R tyrosine kinase activity. The most potent inhibitor of p51ck identified, RPR-108518A [I, R1 = 3,4,5-(MeO)3C6H2, X = NH], has an IC50 of 0.50 μ M. The 3-chlorophenoxy- and 3-chlorothiophenoxy- derivs. I (R1 = 3-ClC6H4, X = O, S) were also shown to be extremely potent EGF-R inhibitors.

IT 146871-70-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and tyrosine kinase inhibitory activity of anilino-, phenoxy-, and thiophenoxy-quinazolines and structure activity)

RN 146871-70-7 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

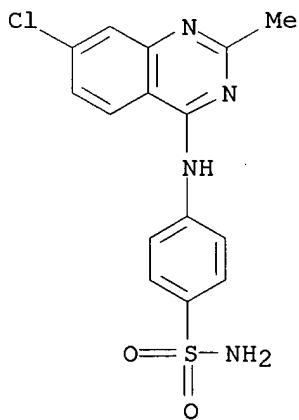
L6 ANSWER 83 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:149164 HCPLUS

DOCUMENT NUMBER: 126:199535

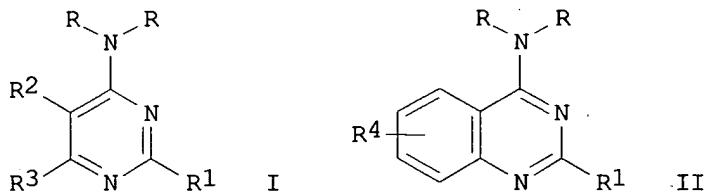
TITLE: Fused pyrimidines. Synthesis of new derivatives of

AUTHOR(S): potential diuretic activity
 Eisa, H. M.; El-Ashmawy, M. B.; Tayel, M. M.; Abo
 El-Magd, S. A.; El-Kashef, H. A.
 CORPORATE SOURCE: Faculty Pharmacy, University Mansoura, Mansoura,
 35516, Egypt
 SOURCE: Bollettino Chimico Farmaceutico (1996), 135(10),
 585-590
 CODEN: BCFAAI; ISSN: 0006-6648
 PUBLISHER: Societa Editoriale Farmaceutica
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Certain derivs. of quinazoline and its bioisostere pyridopyrimidine carrying important structural features that contribute to diuretic activity, such as sulfonamido, morpholino and chlorophenyl, were prepared as potential diuretic agents. Likewise, some tricyclic 1,2,4-triazolo[3,4-b]quinazolines and pyrido[3,2-d][1,2,4]triazolo[4,3-a]pyrimidines with the same features were reported. Nine compds. were tested for diuretic activity in rats and the results showed that the active compound is 7-chloro-2-methyl-3-phthalimido-4(3H)-quinazoline.
 IT 187942-04-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and diuretic activity of pyrimidines and fused pyrimidines)
 RN 187942-04-7 HCPLUS
 CN Benzenesulfonamide, 4-[(7-chloro-2-methyl-4-quinazolinyl)amino]- (9CI)
 (CA INDEX NAME)



L6 ANSWER 84 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:580373 HCPLUS
 DOCUMENT NUMBER: 125:221864
 TITLE: Preparation of 4-aminopyrimidines and
 4-aminoquinazolines
 INVENTOR(S): Zielinski, Wojciech; Mazik, Monika
 PATENT ASSIGNEE(S): Politechnika Slaska, Pol.
 SOURCE: Pol., 5 pp.
 CODEN: POXXA7
 DOCUMENT TYPE: Patent
 LANGUAGE: Polish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|--|----------------------|
| PL 169025 | B1 | 19960531 | PL 1992-296745
PL 1992-296745 | 19921124
19921124 |
| PRIORITY APPLN. INFO.: | | | CASREACT 125:221864; MARPAT 125:221864 | |
| OTHER SOURCE(S): | | | | |
| GI | | | | |



AB The title compds. [I and II; R = H, alkyl, aryl; R1, R3 = alkyl, aryl; R2 = H, alkyl, (substituted) Ph; R4 = H, alkyl, alkoxy, etc.], useful as potential anticancer agents, antihypertensives, antiviral (HIV-1) agents and fungicides (no data), were prepared by reaction of R5N:C(R1)X [R5 = R2CH:CR3, R4C6H4; X = Cl, Cl2P(O), etc.] with R2NC.tplbond.N followed by cyclization of the intermediate R5N:CN:C(X)NR2 (III). Refluxing the intermediate III (R5 = R2CH:CR3) in PhMe afforded compds. I while refluxing III (R5 = R4C6H4) in the presence of Lewis acids such as TiCl4 in C6H6 afforded compds. II.

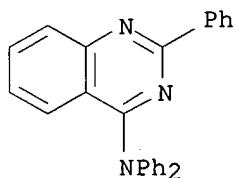
IT 103051-13-4P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of 4-aminopyrimidines and 4-aminoquinazolines)

RN 103051-13-4 HCPLUS

CN 4-Quinazolinamine, N,N,2-triphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 85 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:572296 HCPLUS

DOCUMENT NUMBER: 125:264991

TITLE: Tyrphostins IV-highly potent inhibitors of EGF receptor kinase. Structure-activity relationship study of 4-anilidoquinazolines

AUTHOR(S): Gazit, Aviv; Chen, Jeffrey; App, Harald; McMahon, Gerald; Hirth, Peter; Chen, Irit; Levitzki, Alexander

CORPORATE SOURCE: Alexander Silverman Inst. Life Sci., Hebrew Univ. Jerusalem, Jerusalem, 91904, Israel

SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(8), 1203-1207

PUBLISHER: CODEN: BMECEP; ISSN: 0968-0896

DOCUMENT TYPE: Elsevier

LANGUAGE: Journal

English

AB Potent 4-anilido-substituted quinazolines which potently inhibit epidermal

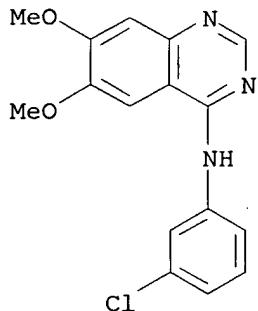
growth factor receptor (EGFR) kinase were prepared. Structure-activity relation studies reveal high sensitivity to substitution at the aniline ring.

IT 170449-18-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation and structure-activity relationship study of anilidoquinazolines as EGF receptor kinase inhibitors)

RN 170449-18-0 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy-, monohydrochloride
(9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 86 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:536936 HCPLUS

Correction of: 1996:73866

DOCUMENT NUMBER: 125:195598

Correction of: 124:232395

TITLE: Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor

AUTHOR(S): Newcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.

CORPORATE SOURCE: Sch. Med., Univ. Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-928
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC_{50} 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC_{50} of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C- γ 1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC_{50} 0.34 and 0.44

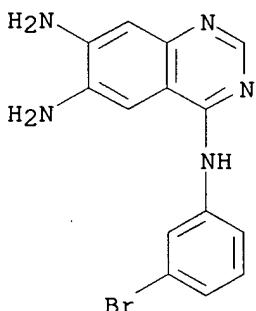
nM) and a pyrroloquinazoline analog (IC₅₀ 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

IT 169205-87-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)

RN 169205-87-2 HCPLUS

CN 4,6,7-Quinazolinetriamine, N4-(3-bromophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 87 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:532223 HCPLUS

DOCUMENT NUMBER: 125:212008

TITLE: Inhibition of the epidermal growth factor receptor tyrosine kinase by PD 153035 in human A431 tumors in athymic nude mice

AUTHOR(S): Kunkel, Mark W.; Hook, Kenneth E.; Howard, Curtis T.; Przybranowski, Sally; Roberts, Billy J.; Elliott, William L.; Leopold, Wilbur R.

CORPORATE SOURCE: Division Warner-Lambert Company, Department Cancer Research, Ann Arbor, MI, 48105, USA

SOURCE: Investigational New Drugs (1996), Volume Date 1995-1996, 13(4), 295-302
 CODEN: INNDDK; ISSN: 0167-6997

PUBLISHER: Kluwer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PD153035 is a potent ($K_i = 6$ pm) and specific inhibitor of the epidermal growth factor (EGF) receptor tyrosine kinase that suppresses tyrosine phosphorylation of the EGF receptor in A431 cells at nanomolar concns. in cell culture. We have examined the pharmacokinetics of this compound and its ability to rapidly suppress phosphorylation of the EGF receptor in A431 human epidermoid tumors grown as xenografts in immunodeficient nude mice. Following a single i.p. dose of 80 mg/kg, the drug levels in the plasma

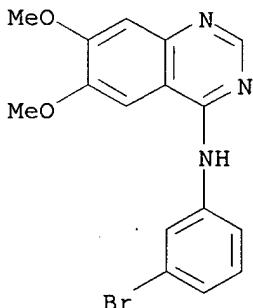
and tumor rose to 50 and 22 μM within 15 min. While the plasma levels of PD153035 fell below 1 μM by 3 h, in the tumors, it remained at micromolar concns. for at least 12 h. The tyrosine phosphorylation of the EGF receptor was rapidly suppressed by 80-90% in the tumors. However, receptor phosphorylation returned to control levels after 3 h despite the continued presence of the drug at concns. which, based on previous *in vitro* results, were predicted to maintain inhibition. EGF-stimulated tyrosine kinase activity in tumor exts. was decreased and recovered in parallel with the effects of PD153035 on receptor phosphorylation; although, the activity had reached only about half of the control activity after three hours. These results demonstrate the potential for using small mol: inhibitors to inhibit the EGF receptor tyrosine kinase *in vivo*; although, a fair evaluation of their potential anti-cancer activity will have to wait for solns. to problems with sustained delivery, which may allow us to maintain suppression of EGF receptor phosphorylation.

IT 153436-54-5, PD 153035

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of epidermal growth factor receptor tyrosine kinase by PD 153035 in human A431 epidermoid tumors in athymic nude mice)

RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 88 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:530427 HCPLUS

DOCUMENT NUMBER: 125:185163

TITLE: Tyrphostin AG 1478 preferentially inhibits human glioma expressing truncated rather than wild-type epidermal growth factor receptors

AUTHOR(S): Han, Yuchun; Caday, Cornelio Gacusana; Nanda, Anil; Cavenee, Webster K.; Huang, H-J.

CORPORATE SOURCE: Biomedical Res. Inst., Louisiana State Univ. Med. Cent., Shreveport, LA, 71130, USA

SOURCE: Cancer Research (1996), 56(17), 3859-3861

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

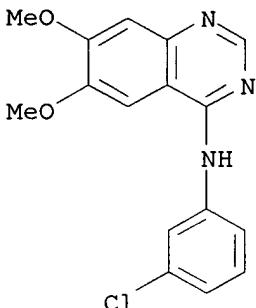
AB The effects of a new epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, tyrphostin AG 1478, were tested on three related human glioma cell lines: U87MG, which expressed endogenous wild-type (weight) EGFR, and two retrovirally infected U87MG cell populations which overexpressed either weight (U87MG.wtEGFR) or truncated EGFR (U87MG. Δ EGFR). Although AG 1478 inhibited cell growth, DNA synthesis, EGFR tyrosine kinase activity, and receptor autophosphorylation of each cell line tyrosine kinase activity, and receptor autophosphorylation of each cell line in a

dose-dependent manner, it was significantly more potent in U87MG.ΔEGFR cells than in the other two cell lines. The increased inhibitory response of U87MG.ΔEGFR cells was due to a greater sensitivity of the constitutively autophosphorylated Mr 140,000 and 155,000 ΔEGFR species to AG 1478. These results suggest that AG 1478 is a relatively specific inhibitor of the ΔEGFR, and this finding may have important therapeutic implications since the ΔEGFR occurs frequently in glioblastomas and in breast, lung, and ovarian cancers.

IT 153436-53-4, Tyrphostin AG 1478
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tyrphostin AG 1478 preferentially inhibits human glioma expressing truncated rather than wild-type epidermal growth factor receptors)

RN 153436-53-4 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

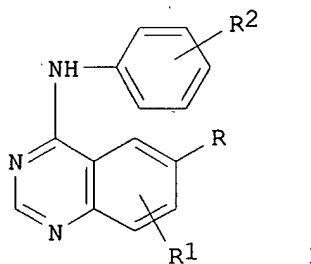


L6 ANSWER 89 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:476843 HCAPLUS
 DOCUMENT NUMBER: 125:142761
 TITLE: Quinazoline derivatives
 INVENTOR(S): Barker, Andrew John
 PATENT ASSIGNEE(S): Zeneca Limited, UK
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9616960 | A1 | 19960606 | WO 1995-GB2768 | 19951128 |
| W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9539330 | A | 19960619 | AU 1995-39330 | 19951128 |
| EP 794953 | A1 | 19970917 | EP 1995-937126 | 19951128 |
| EP 794953 | B1 | 19990506 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10509972 | T | 19980929 | JP 1995-518417 | 19951128 |
| AT 179708 | T | 19990515 | AT 1995-937126 | 19951128 |

| | | | | |
|------------------------|-------------------|----------|----------------|------------|
| US 5955464 | A | 19990921 | US 1997-860088 | 19970522 |
| PRIORITY APPLN. INFO.: | | | GB 1994-24233 | A 19941130 |
| | | | WO 1995-GB2768 | W 19951128 |
| OTHER SOURCE(S): | MARPAT 125:142761 | | | |
| GI | | | | |



AB The invention concerns quinazoline derivs. I ($m = 1, 2$; $R1 = H$, halo, alkyl, alkoxy; $n = 1-3$; $R2 = H$, OH, halo, alkyl; $R = 5-$ or 9-membered nitrogen-linked heteroaryl moiety containing up to four nitrogen heteroatoms, or $R =$ a 5-, 6-, 9- or 10-membered nitrogen-linked unsatd. heterocyclic moiety containing up to three nitrogen heteroatoms which bears one or two substituents selected from oxo and thioxo) and the use of the receptor tyrosine kinase inhibitory properties of the compds. in the treatment of proliferative diseases such as cancer. Among the approx. 15 title compds. prepared, 4-(3-methylanilino)-, 4-(3-chloro-4-fluoroanilino)-, 4-(4-benzoyl-3-chloroanilino)-, and 4-[3-methyl-4-(2-pyridylmethoxy)anilino]-6-(1-imidazolyl)quinazolines were claimed.

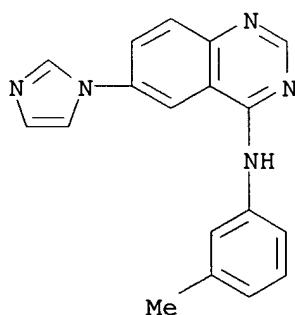
IT 179552-59-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of tyrosine kinase inhibiting imidazolylquinazolines)

RN 179552-59-1 HCPLUS

CN 4-Quinazolinamine, 6-(1H-imidazol-1-yl)-N-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 90 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:462220 · HCPLUS

DOCUMENT NUMBER: 125:114665

TITLE: Preparation of quinoline and quinazoline protein tyrosine kinase inhibitors

INVENTOR(S): Hudson, Alan Thomas; Vile, Sadie; Barraclough, Paul; Franzmann, Karl Witold; McKeown, Stephen Carl; Page, Martin John

PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK

SOURCE: PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

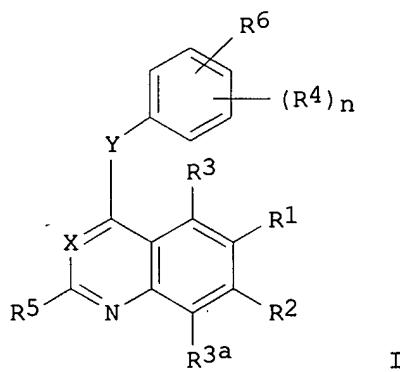
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9609294 | A1 | 19960328 | WO 1995-GB2202 | 19950918 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9534824 | A | 19960409 | AU 1995-34824 | 19950918 |
| ZA 9507853 | A | 19970318 | ZA 1995-7853 | 19950918 |
| EP 782570 | A1 | 19970709 | EP 1995-931351 | 19950918 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10505600 | T | 19980602 | JP 1995-509740 | 19950918 |
| PRIORITY APPLN. INFO.: | | | GB 1994-18852 | A 19940919 |
| | | | GB 1995-7788 | A 19950413 |
| | | | GB 1995-10757 | A 19950526 |
| | | | WO 1995-GB2202 | W 19950918 |

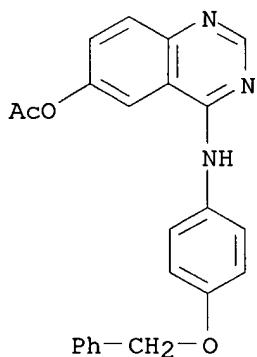
OTHER SOURCE(S): MARPAT 125:114665

GI



AB The title compds. [I; X = N, CH; Y = W(CH₂), (CH₂)W, W; W = O, S(O)m, (un)substituted NH; R1 = NH₂, H, halogen, OH, NO₂, CO₂H, CF₃, CF₃O, ureido, etc.; R4 = H, OH, halogen, alkyl, alkoxy, alkylthio, CN, NO₂, CF₃, etc.; n = 1-3; R5 = H, halogen, CF₃, alkyl, alkoxy; R6 = substituted hydrocarbyl, etc.], which are protein tyrosine kinase inhibitors, are prepared. Thus, 4-chloroquinoline was reacted with 4-methoxyaniline in the presence of HCl, producing 4-(4-phenoxyanilino)quinoline hydrochloride, m.p. 216-218°, which demonstrated a IC₅₀ against p56^{lck} protein tyrosine kinase of 5 μM.

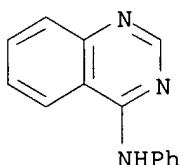
IT 179246-80-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of quinoline and quinazoline protein tyrosine kinase inhibitors)
 RN 179246-80-1 HCAPLUS
 CN 6-Quinazolinol, 4-[4-(phenylmethoxy)phenyl]amino]-, acetate (ester), monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 91 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:312235 HCAPLUS
 DOCUMENT NUMBER: 125:25623
 TITLE: Structure-activity relationships for
 4-anilinoquinazolines as potent inhibitors at the ATP
 binding site of the epidermal growth factor receptor
 in vitro
 AUTHOR(S): Denny, William A.; Newcastle, Gordon W.; Bridges,
 Alexander J.; Fry, David W.; Kraker, Alan J.
 CORPORATE SOURCE: Cancer Research Lab., Univ. Auckland School Medicine,
 Auckland, 92019, N. Z.
 SOURCE: Clinical and Experimental Pharmacology and Physiology
 (1996), 23(5), 424-427
 CODEN: CEXPB9; ISSN: 0305-1870
 PUBLISHER: Blackwell
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Structure-activity relationships are described for the inhibition of the
 tyrosine kinase activity (phosphorylation of a fragment of phospholipase
 C_{g1}) of the epidermal growth factor receptor (EGFR) by
 4-anilinoquinazolines. These compds. are competitive inhibitors at the
 ATP binding site. The preferred side chain is anilino-, substituted at
 the 3-position with small lipophilic groups. The quinazoline moiety is
 absolutely required for activity, but substituents on the quinazoline
 greatly modulate potency, with electron-donating groups favored. The most
 potent analog, the 6,7-dimethoxy derivative, has an IC₅₀ of 29 pmol/L and a
 very high selectivity for the EGFR over other tyrosine kinase enzymes.
 The present study shows that it is possible to identify small mols. that
 are very potent, yet highly selective, inhibitors of a single component of

the growth signal transduction pathway in cells.
 IT 34923-95-0
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (anilinoquinazolines as potent inhibitors at ATP binding site of epidermal growth factor receptor)
 RN 34923-95-0 HCAPLUS
 CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)

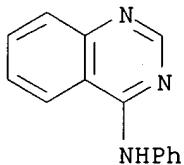


L6 ANSWER 92 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:160721 HCAPLUS
 DOCUMENT NUMBER: 124:249673
 TITLE: Specific inhibition of epidermal growth factor receptor tyrosine kinase by 4-anilinoquinazolines
 AUTHOR(S): Wakeling, A. E.; Barker, A. J.; Davies, D. H.; Brown, D. S.; Green, L. R.; Cartlidge, S. A.; Woodburn, J. R.
 CORPORATE SOURCE: Cancer Research Department, Zeneca Pharmaceuticals, Macclesfield/Cheshire, SK10 4TG, UK
 SOURCE: Breast Cancer Research and Treatment (1996), 38(1), 67-73
 CODEN: BCTR6; ISSN: 0167-6806
 PUBLISHER: Kluwer
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Since the mitogenic action of EGF is mediated by ligand-induced autophosphorylation of the EGF receptor (EGFR), and EGFR is commonly overexpressed in solid human tumors, inhibitors of receptor tyrosine kinase activity (RTK) could prove to be effective antitumor agents. Screening of a compound library using an EGF-RTK enzyme prepared from human tumor derived A431 cells identified a series of potent ($IC_{50} < 1\mu M$) enzyme inhibitors. These inhibitors are quinazolines bearing a variety of substituted anilines at the 4-position. The most potent 4-anilinoquinazolines ($IC_{50} = 20nM$) have small non-polar meta substituents on the aniline ring, and are competitive with ATP and non-competitive with substrate. The growth inhibitory activity of these agents was assessed in vitro using KB cells (human oral squamous tumor) grown in the absence or presence of EGF. A selected compound, 4-(3-chloroanilino)quinazoline (CAQ), inhibited EGF-stimulated growth in a concentration dependent manner and complete blockade was observed at concns. (1-10 μM) which had no effect on basal growth. Selectivity of growth inhibition by CAQ was further exemplified in IGF-1-stimulated KB cells where no effect was detected at concns. which completely blocked EGF-stimulated growth. Similarly, CAQ blocked TGF α -stimulated growth in MCF-7 human breast cancer cells without affecting insulin-stimulated growth. These studies define a novel class of EGF-RTK inhibitors which are also potent and selective inhibitors of EGF-stimulated human tumor cell growth in vitro.
 IT 34923-95-0
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL

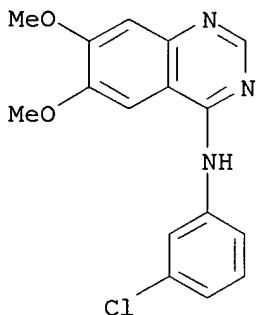
(Biological study); USES (Uses)
 (anilinoquinazolines as specific inhibitors of EGF receptor tyrosine kinase and antineoplastic agents)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 93 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:116898 HCPLUS
 DOCUMENT NUMBER: 124:249905
 TITLE: Inhibition of acute lymphoblastic leukemia by a Jak-2 inhibitor
 AUTHOR(S): Meydan, Naftaly; Grunberger, Tom; Dadi, Harjit;
 Shahar, Michal; Arpaia, Enrico; Lapidot, Zvi; Leeder,
 J. Steven; Freedman, Melvin; Cohen, Amos; et al.
 CORPORATE SOURCE: The Hospital for Sick Children, Univ. Toronto,
 Toronto, M5G 1X8, Can.
 SOURCE: Nature (London) (1996), 379(6566), 645-8
 CODEN: NATUAS; ISSN: 0028-0836
 PUBLISHER: Macmillan Magazines
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Acute lymphoblastic leukemia (ALL) is the most common cancer of childhood. Despite the progress achieved in its treatment, 20% of cases relapse and no longer respond to chemotherapy. The most common phenotype of all cells share surface antigens with very early precursors of B cells and are therefore believed to originate from this lineage. Characterization of the growth requirement of ALL cells indicated that they were dependent on various cytokines, suggesting paracrine and/or autocrine growth regulation. Because many cytokines induce tyrosine phosphorylation in lymphoid progenitor cells, and constitutive tyrosine phosphorylation is commonly observed in B-lineage leukemias, attempts have been made to develop protein tyrosine kinase (PTK) blockers of leukemia cell growth. Here the authors show that leukemic cells from patients in relapse have constitutively activated Jak-2 PTK. Inhibition of Jak-2 activity by a specific tyrosine kinase blocker, AG-490, selectively blocks leukemic cell growth in vitro and in vivo by inducing programmed cell death, with no deleterious effect on normal hematopoiesis. None of the other tyrphostins tested had any activity against leukemic cells.
 IT 153436-53-4, AG 1478
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibition of acute lymphoblastic leukemia by a Jak-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)
 RN 153436-53-4 HCPLUS
 CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 94 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:73866 HCAPLUS

DOCUMENT NUMBER: 124:232395

TITLE: Tyrosine Kinase Inhibitors. 9. Synthesis and Evaluation of Fused Tricyclic Quinazoline Analogs as ATP Site Inhibitors of the Tyrosine Kinase Activity of the Epidermal Growth Factor Receptor

AUTHOR(S): Newcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.

CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-28
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC_{50} 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC_{50} of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C- γ 1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC_{50} s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC_{50} 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

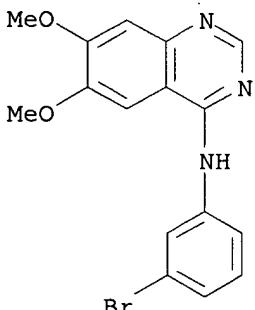
IT 153436-54-5DP, analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
 (preparation of imidazo[4,5-g]quinazoline analogs as tyrosine kinase
 inhibitors)

RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 95 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:20313 HCPLUS

DOCUMENT NUMBER: 124:202145

TITLE: Some reactions of 4-chloro- and 4-hydrazino-2-(α -naphthylmethyl)quinazoline

AUTHOR(S): El-Farargy, A.F.; Hamad, M.M.; Said, S.A.

CORPORATE SOURCE: Faculty of Science, Zagazig University, Zagazig, Egypt

SOURCE: Egyptian Journal of Chemistry (1995), Volume Date
 1993, 36(6), 497-503

CODEN: EGJCA3; ISSN: 0367-0422

PUBLISHER: National Information and Documentation Centre

DOCUMENT TYPE: Journal

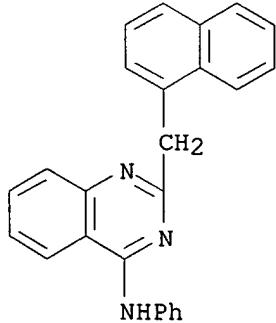
LANGUAGE: English

AB 4-Chloro-2-(α -naphthylmethyl)quinazoline was aminated to give the 4-amino- derivative and was cyclized with compds. such as anthranilic acid to give compds. such as benzopyrimidoquinazolines. 4-Hydrazino-2-(α -naphthylmethyl)quinazoline underwent cyclocondensation with reagents such as Et chlorocarbonate to give triazolo[3,4-a]quinazolines.

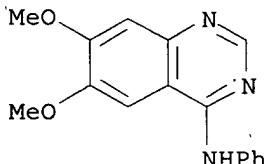
IT 174139-83-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 174139-83-4 HCPLUS

CN 4-Quinazolinamine, 2-(1-naphthalenylmethyl)-N-phenyl- (9CI) (CA INDEX
 NAME)

L6 ANSWER 96 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:18685 HCAPLUS
 DOCUMENT NUMBER: 124:134940
 TITLE: Enantioselective inhibition of the epidermal growth factor receptor tyrosine kinase by 4-(α -phenethylamino)quinazolines
 AUTHOR(S): Bridges, Alexander J.; Cody, Donna R.; Zhou, Hairong; McMichael, Amy; Fry, David W.
 CORPORATE SOURCE: Parke-Davis Pharmaceutical Research Division, Ann Arbor, MI, 48105, USA
 SOURCE: Bioorganic & Medicinal Chemistry (1995), 3(12), 1651-6
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB 4-Benzylaminoquinazolines can be potent reversible inhibitors of the EGFR tyrosine kinase at the ATP binding site. Examination of benzylic methylation reveals that an (R)-Me group is four- to six-fold activating. In sharp contrast, (S)-methylation causes a > 30 to 500-fold loss of inhibitory activity, showing that the ATP-binding site of the receptor has very low tolerance for even moderate out-of-plane bulk in certain directions. It is suggested that the best of these inhibitors can induce a conformation of the kinase not available to poorer inhibitors.
 IT 21561-09-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (enantioselective inhibition of epidermal growth factor receptor tyrosine kinase by 4-(α -phenethylamino)quinazolines)
 RN 21561-09-1 HCAPLUS
 CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



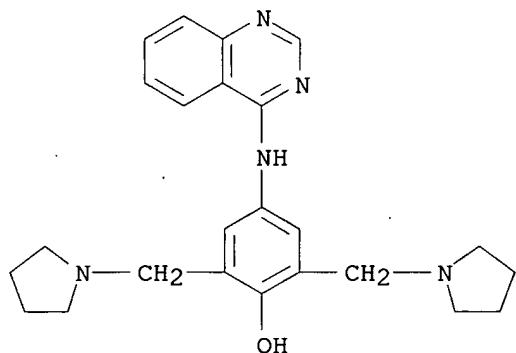
L6 ANSWER 97 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:1004129 HCAPLUS
 DOCUMENT NUMBER: 124:134760
 TITLE: Studies on molecular modification of novel constituents of Chinese medicinal plants
 AUTHOR(S): Ruyun, Ji
 CORPORATE SOURCE: Shanghai Institute Materia Medica, Chinese Academy Sciences, Shanghai, 200031, Peop. Rep. China
 SOURCE: Medicinal Chemistry Research (1995), 5(8), 587-94
 CODEN: MCREEB; ISSN: 1054-2523
 PUBLISHER: Birkhaeuser
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Several novel active principles have been isolated and identified from Chinese herbs in the Shanghai Institute of Materia Medica. The syntheses of huperzine A and edulinine are described here. Numerous new compds. have been synthesized by modification of the structures of the natural constituents. Pharmacol. exams. showed that some of such compds. were biol. active.

IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (biol. activity in relation to mol. modification of novel constituents of Chinese medicinal plants)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 98 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:1002151 HCAPLUS

DOCUMENT NUMBER: 124:176003

TITLE: Substituted 2,4-diaminoquinazolines and
 2,4-diamino-8-alkylpurines as antagonists of the
 neurokinin-2 (NK2) receptor

AUTHOR(S): Jacobs, Robert T.; Mauger, Russell C.; Ulatowski,
 Terrance G.; Aharony, David; Buckner, Carl K.

CORPORATE SOURCE: Dep. Medicinal Chem., Business Unit ZENECA, Inc.,
 Wilmington, DE, 19850-5437, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1995),
 5(23), 2879-84

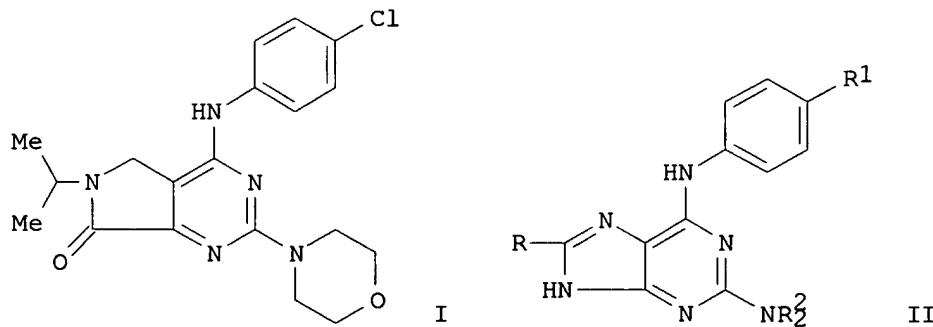
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Modification of the heterocyclic nucleus of a lead pyrrolopyrimidine I, found to be active as an antagonist at the neurokinin-2 (NK2) receptor, is described. Compds. based on the purine nucleus II (R = Me, Et, Pr,

CHMe₂, R1 = Cl, CF₃, NR22 = morpholino, 4-oxopiperidino, NHCH₂Ph, NHBu, etc.) were found to be particularly interesting, and were modified at the C(2), C(4) and C(8) substituents to afford compds. with high potency.

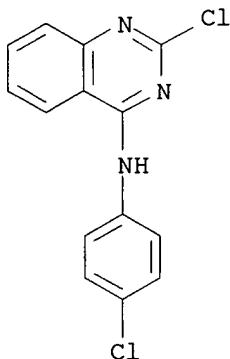
IT 174074-90-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate in preparation of aminoquinazolines with neurokinin-2 receptor antagonist activity)

RN 174074-90-9 HCPLUS

CN 4-Quinazolinamine, 2-chloro-N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 99 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:983167 HCPLUS

DOCUMENT NUMBER: 124:21051

TITLE: Tyrosine kinase inhibitors: unusually steep structure-activity relationship for analogs of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline (PD 153035), a potent inhibitor of the epidermal growth factor receptor

AUTHOR(S): Bridges, Alexander J.; Zhou, Hairong; Cody, Donna R.; Newcastle, Gordon W.; McMichael, Amy; Showalter, H. D. Hollis; Fry, David W.; Kraker, Alan J.; Denny, William A.

CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48106-1047, USA

SOURCE: Journal of Medicinal Chemistry (1996), 39(1), 267-76

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 4-(3-Bromoanilino)-6,7-dimethoxyquinazoline (PD 153035) is a very potent inhibitor (IC₅₀ 0.025 nM) of the tyrosine kinase activity of the EGF receptor, binding competitively at the ATP site. Structure-activity relations for close analogs of PD 153035 are very steep. Some derivs. have IC₅₀ ≤80-fold better than predicted from simple additive binding energies, yet analogs possessing combinations of similar Ph and quinazoline substituents do not show this supra-additive effect. Some substituents which are mildly deactivating by themselves can be strongly activating when used in the correct combinations; therefore, certain substituted analogs may induce a change in conformation of the receptor when they bind. There is some bulk tolerance for substitution in the 6- and 7-positions of the quinazoline, so that PD 153035 is not the optimal inhibitor for the induced conformation. 4-(3-Bromoanilino)-6,7-diethoxyquinazoline shows an IC₅₀ of 0.006 nM, making it the most potent

inhibitor of the tyrosine kinase activity of the EGF receptor yet reported.

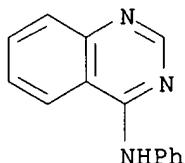
IT 34923-95-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study; unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epidermal growth factor receptor tyrosine kinase inhibitors:
structure-activity relations for analogs of
(bromoanilino)dimethoxyquinazoline (PD 153035))

RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 100 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:926425 HCAPLUS

DOCUMENT NUMBER: 123:329984

TITLE: Receptor tyrosine kinase inhibitors for inhibiting cell proliferative disorders

INVENTOR(S): Chen, Hui; Gazit, Aviv; Hirth, Klaus Peter; Levitzki, Alex; Mann, Elaina; Shawver, Laura K.; Tsai, Jianming; Tang, Peng Cho

PATENT ASSIGNEE(S): Sugen, Inc., USA; Yissum Research Development Co.

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

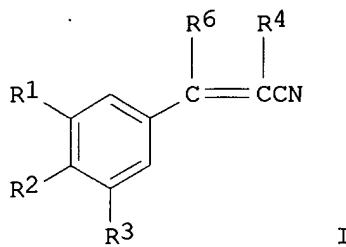
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 9524190 | A2 | 19950914 | WO 1995-US2826 | 19950306 |
| WO 9524190 | A3 | 19951109 | | |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9520968 | A | 19950925 | AU 1995-20968 | 19950306 |
| PRIORITY APPLN. INFO.: | | | US 1994-207933 | A 19940307 |
| | | | WO 1995-US2826 | W 19950306 |
| OTHER SOURCE(S): GI | | MARPAT 123:329984 | | |



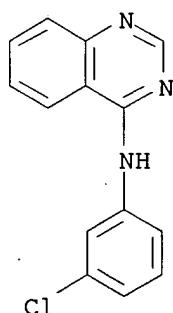
AB Receptor tyrosine kinase inhibitors I [R1-R3, R6 = alkyl, alkenyl, alkynyl, alkoxy, OH, amino, SH, alkylthio, halo, H, NO₂, etc.; R4 = C(S)NHR₅, C(O)NHR₅, SO₂YR₅; Y = single bond, C(CN):CH:CH, azaalkyl; R₅ = (substituted) aralkyl, CN] and II [R7-R10 = R1-R3 above; R12 = C(O)Me, C(S)Me, C(O)CF₃, C(S)CF₃; R13 = aryl, alkylaryl] are prepared for use in treating cell proliferative disorders such as cancers characterized by overactivity or inappropriate activity of HER2 receptors or EGF receptors. Thus, I [R1, R2 = OH, R3 = I, R4 = C(O)NH(CH₂)₃Ph, R6 = H] (III) was prepared in 2 steps by condensation of 5-iodovanillin with N-(3-phenylpropyl)cyanoacetamide. III inhibited EGF receptor kinase activity in EGC7 cells, HER2 kinase activity in BT-474 cells, and platelet-derived growth factor receptor kinase β activity with an IC₅₀ of 4, 18, and 35 μM, resp., and inhibited growth of SKBR3 and SKOV3 cells in vitro at IC₅₀ 9 and 4.5 μM, resp.

IT 88404-44-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(receptor tyrosine kinase inhibitors for inhibiting cell proliferative disorders)

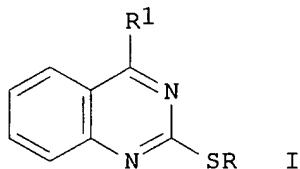
RN 88404-44-8 HCPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 101 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:904680 HCPLUS
DOCUMENT NUMBER: 124:117223
TITLE: New 2-(alkylthio)-4-chloro(and amino)quinazolines
AUTHOR(S): Abdullaev, N. P.; Umarov, A.; Obidov, U. O.; Shokhidoyatov, Kh. M.
CORPORATE SOURCE: Inst. Khim. Rastit. Veshchestv, Uzbekistan
SOURCE: Doklady Akademii Nauk Respublikii Uzbekistan (1994), (12), 24-6
CODEN: DARUEE

PUBLISHER: Fan
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI



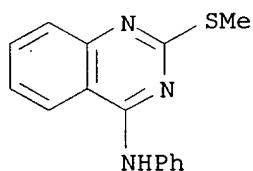
AB Twenty new title compds. I (R = C1-C9 n-alkyl, benzyl; R1 = Cl, NPh, NHCH₂Ph, morpholino, piperidino) are prepared by reaction of 2-(alkylthio)quinazolin-4-ones with POCl₃ and then with amines. I (R1 = substituted amino) were obtained as the hydrochlorides.

IT 172984-20-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of 2-(alkylthio)-4-chloro(and amino)quinazolines)

RN 172984-20-2 HCPLUS

CN 4-Quinazolinamine, 2-(methylthio)-N-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

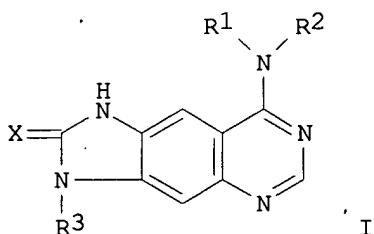
L6 ANSWER 102 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:846525 HCPLUS
 DOCUMENT NUMBER: 123:256749
 TITLE: Preparation of imidazoquinazoline derivatives having cyclic guanosine 3',5'-monophosphate (cGMP)-specific phosphoesterase inhibitor activity
 INVENTOR(S): Machii, Daisuke; Matsuno, Kenji; Kinoshita, Iwao; Nomoto, Yuji; Takai, Haruki; Ohno, Tetuji; Nagashima, Ken; Ishikawa, Tomoko; Yamada, Koji; et al.
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 9506648 | A1 | 19950309 | WO 1994-JP1456 | 19940902 |
| W: CA, JP, US | | | | |

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 CA 2148082 A1 19950309 CA 1994-2148082 19940902
 EP 668280 A1 19950823 EP 1994-925621 19940902
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
 US 5661147 A 19970826 US 1995-424274 19950426
 PRIORITY APPLN. INFO.: JP 1993-219595 A 19930903
 WO 1994-JP1456 W 19940902

OTHER SOURCE(S): MARPAT 123:256749

GI



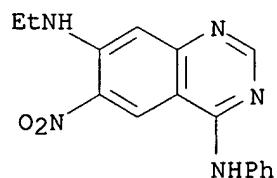
AB Imidazoquinazoline derivs. represented by formula [I; R1, R2 = H, (un)substituted lower alkyl, cycloalkyl, bicycloalkyl, (un)substituted benzocycloalkyl, lower alkenyl, (un)substituted aryl, ring-(un)substituted aromatic heterocyclalkyl, aromatic heterocyclyl, or aralkyl; or NR1R2 = (un)substituted heterocyclyl; R3 = H, lower alkyl, cycloalkyl, lower alkenyl, ring-(un)substituted aryl, aromatic heterocyclalkyl, aromatic heterocyclyl, or aralkyl presents hydrogen, lower alkyl, cycloalkyl alkenyl; X = O, S] or pharmacol. acceptable salts thereof are prepared. These compds. have a potent and selective cGMP-specific PDE inhibitor activity and are useful for treating or mitigating cardiovascular diseases such as thrombosis, angina pectoris, hypertension and arteriosclerosis, asthma and so forth. Thus, 4-benzylamino-7-ethylamino-6-nitroquinazoline (preparation given) was hydrogenated in the presence of 10% Pd-C in DMF at room temperature for 5 h and 50° for 1 h to give 95.2% 6-amino-4-benzylamino-7-ethylaminoquinazoline which was cyclocondensed with N,N-carbonyldiimidazole in DMF at 100° for 3.5 h to give 47.3% I (X = O, R1 = CH₂Ph, R2 = H, R3 = Et). I (X = S, R1 = CH₂Ph, R2 = H, R3 = Et) in vitro showed IC₅₀ of 0.18, 1, 100, and >10,000 nM against PDE V (cGMP-specific phosphoesterase), PDE III (cGMP-inhibited cAMP-specific phosphoesterase), and PDE IV (cAMP-specific phosphoesterase), resp., and at 30 µg/kg i.v. in vivo lowered the median blood pressure by maximum 51.2% in guinea pigs.

IT 168761-67-9P

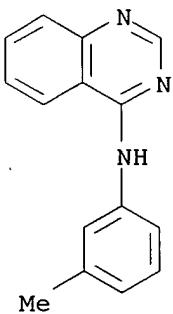
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate for preparation of imidazoquinazoline derivs. as cGMP-specific phosphoesterase inhibitors)

RN 168761-67-9 HCAPLUS

CN 4,7-Quinazolinediamine, N7-ethyl-6-nitro-N4-phenyl- (9CI) (CA INDEX NAME)



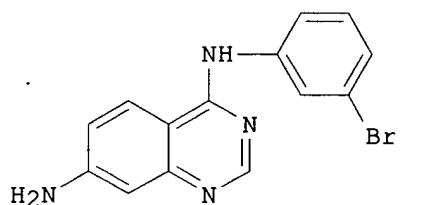
L6 ANSWER 103 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:762714 HCPLUS
 DOCUMENT NUMBER: 123:217852
 TITLE: Observations arising from the use of pure antiestrogens on estrogen-responsive (MCF-7) and estrogen growth-independent (K3) human breast cancer cells
 AUTHOR(S): Nicholson, R. I.; Gee, J. M. W.; Francis, A. B.; Manning, D. L.; Wakeling, A. E.; Katzenellenbogen, B. S.
 CORPORATE SOURCE: Breast Cancer Unit, Tenovus Cancer Research Centre, Cardiff, CF4 4XX, UK
 SOURCE: Endocrine-Related Cancer (1995), 2(1), 115-21
 CODEN: ERCAE9; ISSN: 1351-0088
 PUBLISHER: Journal of Endocrinology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The authors describe a number of the properties exhibited by pure antiestrogens in estrogen-responsive MCF-7 human breast cancer cells and in the estrogen growth-independent variant K3 cells. It is shown that the importance of estrogen receptor-mediated signaling is retained in the basal growth responses of estrogen growth-independent K3 cells. Limited data is presented on the growth-inhibitory properties of aniloquinazoline, a tyrosine kinase inhibitor which shows specificity for epidermal growth factor receptor signaling. It was shown that transforming growth factor α (TGF α) may impinge on estrogen receptor-mediated growth and circumvent the need for high estrogen levels. Pure antiestrogens antagonize estrogen receptor-mediated effects in Wt and K3 cells, possibly by decreasing estrogen receptor and TGF α levels and thereby decreasing cross-talk between these growth-signaling pathways.
 IT 111157-71-2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (observations arising from use of pure antiestrogens on estrogen-responsive (MCF-7) and estrogen growth-independent (K3) human breast cancer cells in relation to estrogen receptors)
 RN 111157-71-2 HCPLUS
 CN 4-Quinazolinamine, N-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 104 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:746894 HCPLUS
 DOCUMENT NUMBER: 123:256632
 TITLE: Tyrosine kinase inhibitors. 5. Synthesis and structure-activity relationships for 4-[(phenylmethyl)amino]- and 4-

(phenylamino)quinazolines as potent adenosine 5'-triphosphate binding site inhibitors of the tyrosine kinase domain of the epidermal growth factor receptor.

AUTHOR(S): Newcastle, Gordon W.; Denny, William A.; Bridges, Alexander J.; Zhou, Hairong; Cody, Donna R.; McMichael, Amy; Fry, David W.
 CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, N. Z.
 SOURCE: Journal of Medicinal Chemistry (1995), 38(18), 3482-7
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 123:256632
 GI

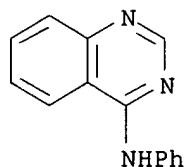


AB A series of 4-substituted quinazolines and related compds. have been prepared and evaluated for their ability to inhibit the tyrosine kinase activity of the epidermal growth factor receptor on a phospholipase C- γ 1-derived substrate. The results show a narrow structure-activity relationship (SAR) for the basic ring system, with quinazoline being the preferred chromophore and benzylamino and anilino the preferred side chains. 4-Chloro-7-nitroquinazoline was heated with 3-bromoaniline and 3-bromoaniline hydrochloride in Me₂CHOH to give 94% 4-[(3-bromophenyl)amino]-7-nitroquinazoline. Reflux of the latter with Fe in EtOH/AcOH gave 90% 7-amino-4-[(3-bromophenyl)amino]quinazoline(I). I inhibited phosphorylation of a 14 residue fragment of phospholipase C- γ 1 by epidermal growth factor receptor with IC₅₀ = 0.1 nM.

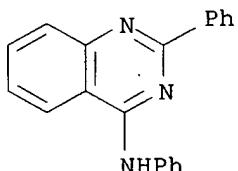
IT 34923-95-0P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of 4-[(phenylmethyl)amino]- and 4-(phenylamino)quinazolines and related compds. as potent binding site inhibitors of the tyrosine kinase domain of the epidermal growth factor receptor)

RN 34923-95-0 HCPLUS

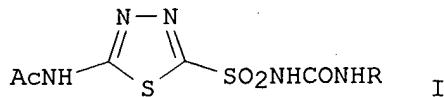
CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1995:746792 HCPLUS
 DOCUMENT NUMBER: 123:132021
 TITLE: Discovery of Potent Cyclic GMP Phosphodiesterase Inhibitors. 2-Pyridyl- and 2-Imidazolylquinazolines Possessing Cyclic GMP Phosphodiesterase and Thromboxane Synthesis Inhibitory Activities
 AUTHOR(S): Lee, Sung J.; Konishi, Yoshitaka; Yu, Dingwei T.; Miskowski, Tamara A.; Riviello, Christopher M.; Macina, Orest T.; Frierson, Manton R.; Kondo, Kigen; Sugitani, Masafumi; et al.
 CORPORATE SOURCE: Biofor Inc., Waverly, PA, 18471, USA
 SOURCE: Journal of Medicinal Chemistry (1995), 38(18), 3547-57
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Moderate cyclic GMP phosphodiesterase (cGMP-PDE, PDE V) inhibitor 2-phenyl-4-anilinoquinazoline (I) was identified utilizing MultiCASE assisted drug design (MCADD) technol. Modification of I was conducted at the 2-, 4-, and 6-positions of the quinazoline ring for enhancement of cGMP-PDE inhibitory activity. The 6-substituted 2-(imidazol-1-yl)quinazolines are 1000 times more potent in in vitro PDE V enzyme assay than the well-known inhibitor zaprinast. The 6-substituted derivs. of 2-(3-pyridyl)quinazoline and 2-(imidazol-1-yl)quinazoline exhibited more than 1000-fold selectivity for PDE V over the other four PDE isoenzymes. In addition, 3 cGMP-PDE inhibitors were found to have an addnl. property of thromboxane synthesis inhibitory activity.
 IT 40288-70-8, 4-Anilino-2-phenylquinazoline
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (pyridyl- and imidazolylquinazolines as cyclic GMP phosphodiesterase and thromboxane synthesis inhibitors)
 RN 40288-70-8 HCPLUS
 CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 106 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:739898 HCPLUS
 DOCUMENT NUMBER: 123:339790
 TITLE: N1,N3-Diaryl sulfonylureas as possible anticancer agents
 AUTHOR(S): Youssef, Khairia M.; Shouman, Samia
 CORPORATE SOURCE: Dep. of Organic Chemistry, Cairo Univ., Cairo, Egypt
 SOURCE: Alexandria Journal of Pharmaceutical Sciences (1994), 8(3), 223-5
 CODEN: AJPSES; ISSN: 1110-1792
 PUBLISHER: University of Alexandria, Faculty of Pharmacy
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB This study describes the synthesis of a number of Sulofenur thiadiazole analogs, e.g. I [R = (un)substituted Ph, 2-naphthyl]. Two different methods were adopted in order to prepare the target compds. The new compds. were evaluated for in vitro cytotoxic activity. Two compds. showed 100% activity against Ehrlich ascites tumor cells.

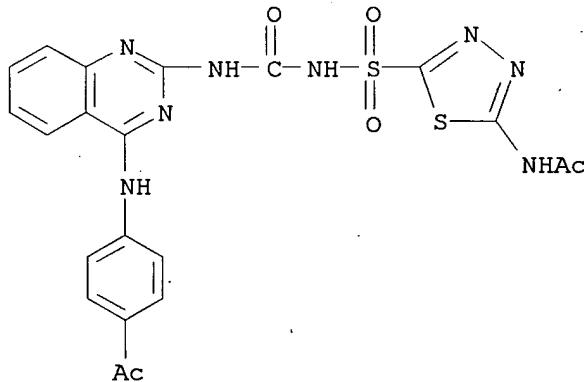
IT 170648-55-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and antitumor activity of N1,N3-diarylsulfonyleureas)

RN 170648-55-2 HCPLUS

CN Acetamide, N-[5-[[[4-[(4-acetylphenyl)amino]-2-quinazolinyl]amino]carbonyl]amino]sulfonyl]-1,3,4-thiadiazol-2-yl]- (9CI)
(CA INDEX NAME)



L6 ANSWER 107 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:666999 HCPLUS

DOCUMENT NUMBER: 123:285897

TITLE: Reversible Inhibitors of the Gastric (H+/K+)-ATPase.
5. Substituted 2,4-Diaminoquinazolines and
Thienopyrimidines

AUTHOR(S): Ife, Robert J.; Brown, Thomas H.; Blurton, Peter;
Keeling, David J.; Leach, Colin A.; Meeson, Malcolm
L.; Parsons, Michael E.; Theobald, Colin J.

CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals R D, Frythe/

Welwyn/ Herts, AL6 9AR, UK

SOURCE: Journal of Medicinal Chemistry (1995), 38(14), 2763-73
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Quinazolines bearing a secondary [4-(arylarnino)] substituent demonstrate a structure-activity relationship for inhibition of the gastric (H+/K+)-ATPase different from the previously described 3-acylquinolines,

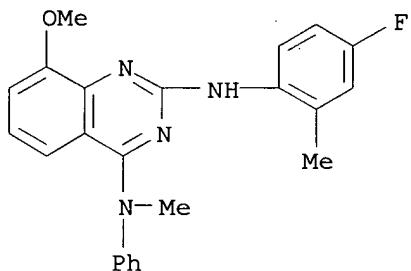
suggesting that, although these compds. are also K⁺-competitive, they probably bind to the enzyme in a different orientation. Compds. bearing a tertiary 4-(aryl amino) substituent, however, in particular 4-(N-methylaryl amino), appear to possess an structure-activity relationship quite similar to the 3-acylquinolines. Compds. possessing both a 4-(N-methylaryl amino) substituent and a 2-(aryl amino) substituent proved to be very potent, K⁺-competitive inhibitors of K⁺-stimulated ATPase activity with Ki values down to 12 nM. Some compds. also proved to be effective inhibitors of stimulated acid secretion in both the rat and dog when dosed i.v. However, although a number of these demonstrated activity after oral administration in dogs, the level and variability precluded further evaluation.

IT 124309-62-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2,4-quinoazolininediamines as gastric ATPase-inhibitors)

RN 124309-62-2 HCPLUS

CN 2,4-Quinazolininediamine, N2-(4-fluoro-2-methylphenyl)-8-methoxy-N4-methyl-N4-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 108 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:604652 HCPLUS
 DOCUMENT NUMBER: 123:25436
 TITLE: Electrophysiological effects of changrolin, an antiarrhythmic agent derived from Dichroa febrifuga, on guinea pig and rabbit heart cells
 AUTHOR(S): Lu, Ling-Ling; Habuchi, Yoshizumi; Tanaka, Hideo; Morikawa, Junichiro
 CORPORATE SOURCE: Dep. Physiol., Kyoto Prefectural Univ. Medicine, Kyoto, Japan
 SOURCE: Clinical and Experimental Pharmacology and Physiology (1995), 22(5), 337-41
 CODEN: CEXPB9; ISSN: 0305-1870
 PUBLISHER: Blackwell
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The electrophysiol. effects of changrolin (CRL), a Chinese antiarrhythmic drug derived from a traditional antimalarial plant were examined using the whole-cell patch-clamp method on single cells isolated from guinea-pig and rabbit hearts. At a clin. relevant concentration of 50 μmol/L changrolin inhibited IC_a by 19.3 ± 6.0% and 17.3 ± 2.6% in guinea-pig and rabbit ventricular cells, resp. The voltage-dependent channel

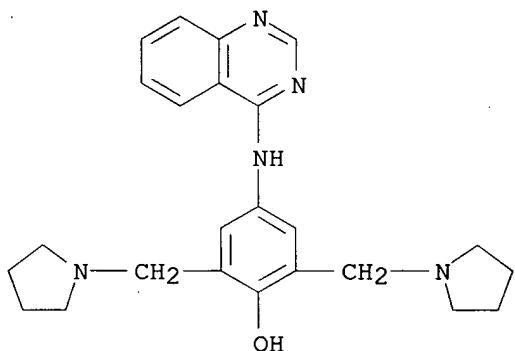
availability curve was not affected. The CRL effect was enhanced to a small extent during repetitive stimulation at 2 Hz. INa was resistant to CRL and the channel availability curve was also unaffected. A small use-dependent inhibition was observed only when the INa was elicited at 5 Hz in the presence of 300 $\mu\text{mol/L}$ CRL. At 50 $\mu\text{mol/L}$, CRL did not affect the time-independent inward rectifier and the delayed rectifier K⁺ currents (IK1 and IK, resp.), but inhibited the transient outward current (ITO) by 17.7 \pm 2.4%. Changrolin significantly shortened the action potential duration in both guinea-pig and rabbit ventricular cells. In conclusion, CRL inhibits ICa and ITO but has little effect on INa.

IT 72063-47-9, Changrolin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(electrophysiolog. effects of changrolin antiarrhythmic from Dichroa febrifuga on heart cells)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 109 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:416613 HCPLUS

DOCUMENT NUMBER: 123:198719

TITLE: Synthesis and antimicrobial activity of certain chalcone derivatives.

AUTHOR(S): Abdou, N. A.; Youssef, K. M.; Kandeel, M. M.; Soliman, L. N.

CORPORATE SOURCE: Faculty Pharmacy, Cairo University, Cairo, Egypt

SOURCE: Bulletin of the Faculty of Pharmacy (Cairo University) (1993), 31(3), 361-7

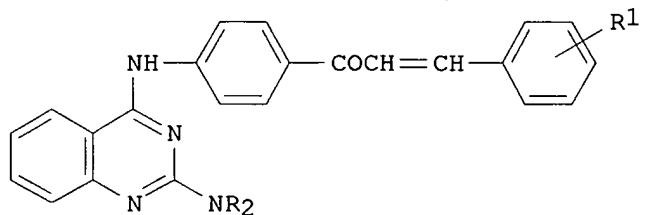
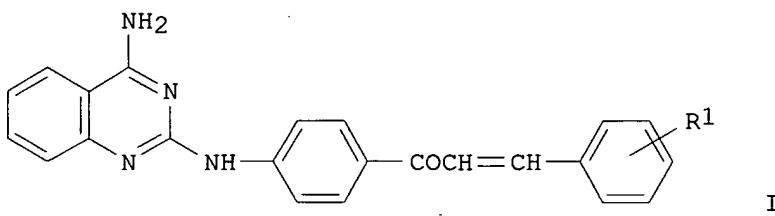
CODEN: BFPHA8; ISSN: 1110-0931

PUBLISHER: Cairo University, Faculty of Pharmacy

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The title compds. I ($R = H, 3\text{-Br}, 4\text{-Cl}$, etc.) and II ($NR_2 = NH_2$, pyrrolidino, morpholino, piperidino; $R^1 = 3\text{-Br}, 4\text{-MeO}, 2\text{-Cl}$, etc.) were prepared from 2,4-dichloroquinazoline and tested for bactericidal and fungicidal activity.

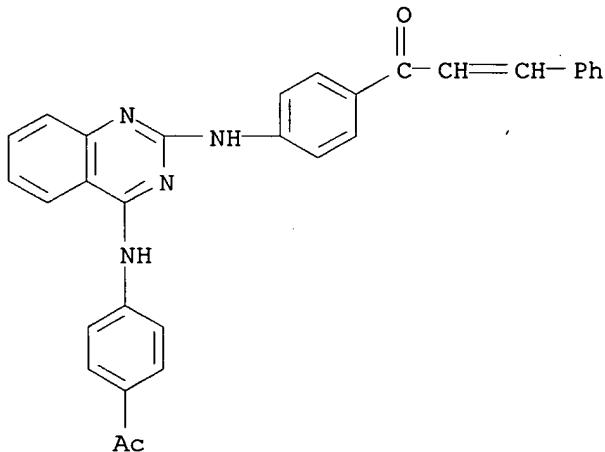
IT 167266-53-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antimicrobial activity of chalcone derivs.)

RN 167266-53-7 HCPLUS

CN 2-Propen-1-one, 1-[4-[(4-acetylphenyl)amino]-2-quinazolinyl]amino]phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 110 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:308750 HCPLUS

DOCUMENT NUMBER: 122:81394

TITLE: Preparation of 2,4-diaminoquinazolines

INVENTOR(S): Ooishi, Akihiro; Yasumoto, Masahiko; Goto, Midori; Tsuchi, Tooru; Shibuya, Isao; Taguchi, Yoichi

PATENT ASSIGNEE(S): Kogyo Gijutsuin, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

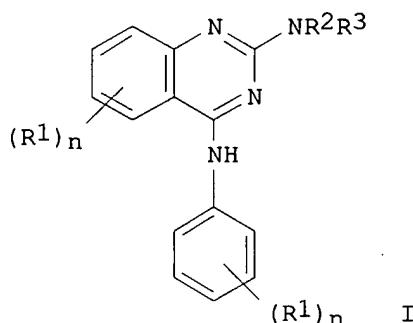
Japanese

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|--------------------------------------|-----------------|----------|
| JP 06263744 | A | 19940920 | JP 1993-78911 | 19930312 |
| PRIORITY APPLN. INFO.: | | | JP 1993-78911 | 19930312 |
| OTHER SOURCE(S): | | CASREACT 122:81394; MARPAT 122:81394 | | |
| GI | | | | |

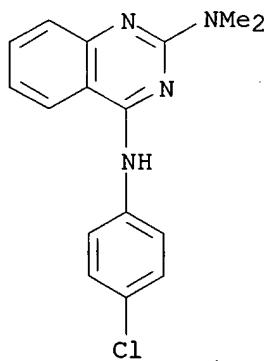


AB The title compds. I.(HX)_m [R₁ = substituent; n = 0 - 4; R₂, R₃ = substituent; or NR₂R₃ = ring; HX = inorg. or organic acid; m = 0 or 1] are prepared by reaction of phenylisothiocyanates with cyanamides under high pressure, followed by treatment with acid. A mixture of phenylisothiocyanate and N,N-dimethylcyanamide was kept at 100° (pressure 800 MPa) for 20 h to give 2-dimethylamino-4-(N-phenylamino)quinazoline (II) which was treated with HCl to give II.HCl. The yield of II.HCl was 86%.

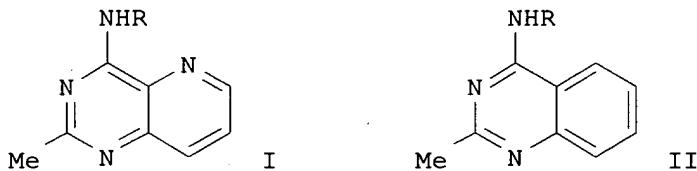
IT 160415-93-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of diaminoquinazolines)

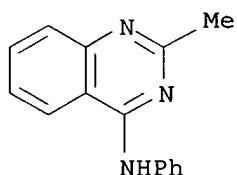
RN 160415-93-0 HCPLUS

CN 2,4-Quinazolinediamine, N4-(4-chlorophenyl)-N₂,N₂-dimethyl- (9CI) (CA INDEX NAME)

L6 ANSWER 111 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:112707 HCAPLUS
 DOCUMENT NUMBER: 122:207621
 TITLE: Cytokinin activity of 4-aminopyridopyrimidines toward
 the growth of tobacco callus
 AUTHOR(S): Nishikawa, Shiro; Maki, Shinji; Nishikimi, Yoshio;
 Kumazawa, Zenzaburo; Kashimura, Naoki
 CORPORATE SOURCE: Fac. Bioresources, Mie Univ., Mie, 514, Japan
 SOURCE: Bioscience, Biotechnology, and Biochemistry (1994),
 58(9), 1709-10
 CODEN: BBBIEJ; ISSN: 0916-8451
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

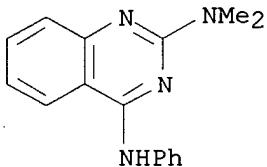


- AB The cytokinin activity of a series of 4-aminopyridopyrimidines (e.g., I, R = CH₂Ph, Ph, isoamyl) and 4-aminoquinazoline (II) was tested on tobacco callus. Among the derivs., 2-methyl-4-anilinopyrido[3,4-d]pyrimidine exhibited moderate activity almost comparable to that of kinetin. The position of the nitrogen atom in the pyridine moiety of the pyridopyrimidine ring was critical for this activity.
- IT 57942-18-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and cytokinin activity in tobacco callus growth)
- RN 57942-18-4 HCAPLUS
 CN 4-Quinazolinamine, 2-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 112 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:94187 HCAPLUS
 DOCUMENT NUMBER: 122:265326
 TITLE: Synthesis of novel 4-(arylarnino)-2-(dialkylamino)quinazolines under high pressure
 AUTHOR(S): Oishi, Akihiro; Yasumoto, Masahiko; Goto, Midori;
 Tsuchiya, Tohru; Shibuya, Isao; Taguchi, Yoichi
 CORPORATE SOURCE: National Inst. Materials Chem. Res., Ibaraki, 305,
 Japan
 SOURCE: Heterocycles (1994), 38(9), 2073-9
 CODEN: HTCYAM; ISSN: 0385-5414
 DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 122:265326
 AB Novel 4-(arylarnino)-2-(dialkylamino)quinazolines (salt) were obtained in good yield by reaction of dialkylcyanamides with 4-substituted Ph isothiocyanates at 800 MPa. The mol. structure of 6-chloro-4-[4-(chlorophenyl)amino]-2-(dimethylamino)quinazoline 2-chlorobenzoate was determined by x-ray crystallog. anal.
 IT 160415-96-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of novel 4-(arylarnino)-2-(dialkylamino)quinazolines under high pressure)
 RN 160415-96-3 HCPLUS
 CN 2,4-Quinazolinediamine, N₂,N₂-dimethyl-N₄-phenyl-, monohydrochloride (9CI)
 (CA INDEX NAME)



● HCl

L6 ANSWER 113 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1994:671425 HCPLUS
 DOCUMENT NUMBER: 121:271425
 TITLE: Epidermal growth factor receptor tyrosine kinase.
 Investigation of catalytic mechanism, structure-based searching and discovery of a potent inhibitor
 AUTHOR(S): Ward, Walter H. J.; Cook, Peter N.; Slater, Anthony M.; Davies, D. Huw; Holdgate, Geoffrey A.; Green, Leslie R.
 CORPORATE SOURCE: ZENECA Pharmaceuticals, Mereside/Alderley Park/Macclesfield/Cheshire, SK10 4TG, UK
 SOURCE: Biochemical Pharmacology (1994), 48(4), 659-66
 CODEN: BCPA6; ISSN: 0006-2952
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Inhibition of tyrosine kinases is a possible approach for the treatment of cancer. We have investigated the catalytic mechanism of the epidermal growth factor receptor tyrosine kinase (EGF-RTK) in order to obtain information for use in structure-based searching for inhibitors. Initial rate studies imply that EGF-RTK forms a ternary complex together with ATP and peptide substrate. Investigation of pH and temperature dependence suggests that the kinase reaction requires the ionized form of a carboxylate (pK = 6.3) and the protonated form of another group (pK = 9.1). These characteristics are consistent with a mechanism where the carboxylate of Asp813(pK = 6.3) facilitates deprotonation of the tyrosyl hydroxyl of the peptide substrate, activating it as a nucleophile to attack the phosphorus of ATP which interacts with a protonated enzyme side-chain (pK = 9.1), possibly the guanidinium group of Arg817. This proposed catalytic mechanism was used to define a query when searching for inhibitors in a database of predicted three-dimensional structures. The procedure involved searching for compds. that mimic the ATP γ -phosphate, tyrosyl hydroxyl and the tyrosyl aromatic ring, all of which seem to interact

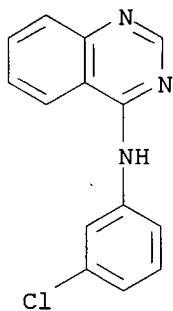
strongly with the enzyme during catalysis. This search allowed identification of inhibitors of EGF-RTK which were used to define queries for two-dimensional searching of a larger database, leading to the discovery of 4-(3-chloroanilino)quinazoline (CAQ) which is a potent inhibitor ($K_i = 16$ nM) of the enzyme. The compound is believed to be the first representative from a new structural class of anilinoquinazoline tyrosine kinase inhibitors. It follows competitive kinetics with respect to ATP and noncompetitive kinetics when the peptide is varied, implying that it functions as an analog of ATP. CAQ is a novel and potent lead in the search for tyrosine kinase inhibitors as potential agents for the treatment of cancer.

IT 88404-44-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (epidermal growth factor receptor tyrosine kinase inhibitors as possible neoplasm inhibitors)

RN 88404-44-8 HCAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 114 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:569777 HCAPLUS

DOCUMENT NUMBER: 121:169777

TITLE: Determination of the molecular mechanical parameters in sulfonamide changrolin compounds as antiarrhythmics

AUTHOR(S): Wang, Qin-Mi; Fan, Yu-Guo; Li, Shu-Shen; Chen, Kai-Kian

CORPORATE SOURCE: Key Lab. Mol. Spectra Struct., Jilin Univ., Changchun, 130023, Peop. Rep. China

SOURCE: Gaodeng Xuexiao Huaxue Xuebao (1994), 15(4), 596-9
 CODEN: KTHPDM; ISSN: 0251-0790

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

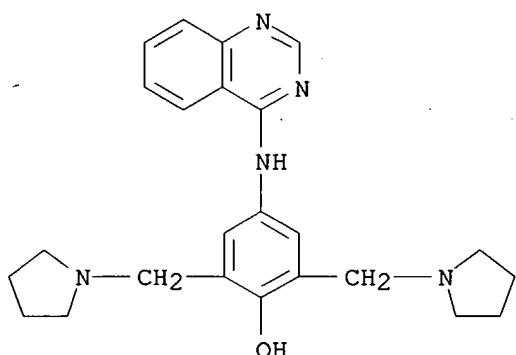
AB Using quantum mechanics MNDO program and mol. mechanics MMP2 program, we determined some unknown mol. mech. parameters in sulfonamide compds. Using these parameters, we calculated a few antiarrhythmic sulfonamide changrolin compds. whose crystal structures are known. We compared the calculated structures with the real structures and the result is satisfactory. All above proves that the obtained parameters are right and usable, and provides a powerful reference for calculating this kind of structures.

IT 72063-47-9D, Changrolin, sulfonamide derivs.

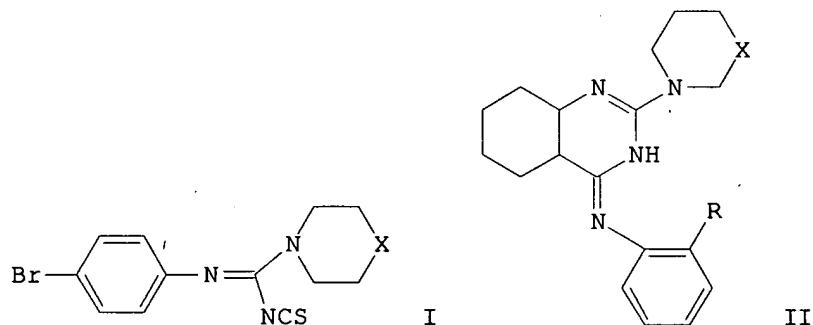
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(determination of mol. mech. parameters in sulfonamide changrolin compds. as antiarrhythmics)

RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 115 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1994:217607 HCAPLUS
 DOCUMENT NUMBER: 120:217607
 TITLE: Amidinoyl isothiocyanates in the synthesis of condensed heterocycles. Preparation of quinazolino[3,4-c][1,3,5]-benzotriazepines and quinazolino[3,4-c][1,2,3,5]-benzotetraazepines
 AUTHOR(S): Stankovsky, S.; Derer, T.; Spirkova, K.
 CORPORATE SOURCE: Fac. Chem. Technol., Slovak Tech. Univ., Bratislava, Slovakia
 SOURCE: Monatshefte fuer Chemie (1993), 124(6-7), 733-8
 DOCUMENT TYPE: CODEN: MOCMB7; ISSN: 0026-9247
 LANGUAGE: English
 GI



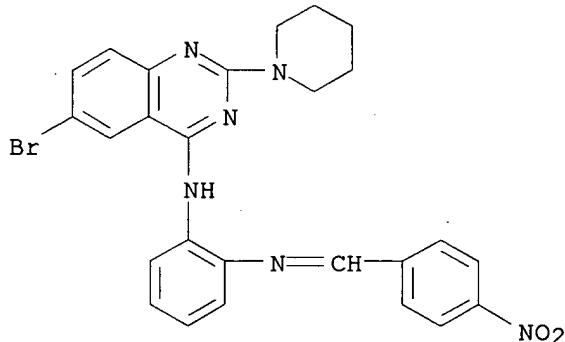
AB When heated, amidinoyl isothiocyanates (I; X = CH, O) with 2-nitrophenyl isothiocyanate cyclize to 4-(2'-nitroanilino)quinazolines (II; R = NO2, X = CH, O) and after reduction to 2'-amino derivs. (II; R = NO2, X = CH, O). The latter serve as precursors to derivs. of the title compds.

IT 153991-69-6P

RL: PREP (Preparation)
 (formation in synthesis of condensed heterocycles,
 quinazolinobenzotriazepines and quinazolinobenzotetraazepines via
 cyclization of isothiocyanates)

RN 153991-69-6 HCAPLUS

CN 1,2-Benzenediamine, N-[6-bromo-2-(1-piperidinyl)-4-quinazolinyl]-N'-(4-nitrophenyl)methylene] - (9CI) (CA INDEX NAME)



L6 ANSWER 116 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:124469 HCPLUS

DOCUMENT NUMBER: 120:124469

TITLE: The effects of cibenzoline and changrolin and their combination on experimental arrhythmias

AUTHOR(S): Li, Mei; Zhang, Jingling; Zhang, Caili

CORPORATE SOURCE: Dep. Pharmacol., Tianjin Med. Coll., Tianjin, 300070, Peop. Rep. China

SOURCE: Tianjin Yiyao (1993), 21(8), 460-3

CODEN: TIYADG; ISSN: 0253-9896

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

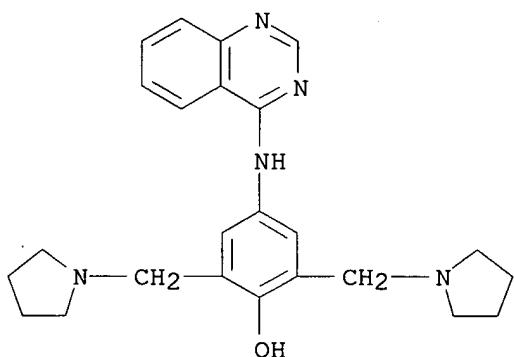
AB The effects of cibenzoline, changrolin and combination of two drugs on aconitine induced arrhythmias in rats were studied. Different doses of cibenzoline or changrolin i.v. could delay the onset time of arrhythmias, resp., and the results had significant difference comparing with the control group. The combination of 1 mg/kg cibenzoline and 0.7 mg/kg changrolin i.v., presented potentiated effects in anti-ventricular flutter and fibrillation. Compared with the control group, cibenzoline 0.5 mg/kg or changrolin 0.7 mg/kg i.v., singly had no significantly difference on the doses of aconitine to induce the ventricular premature systole and fibrillation, but when those two drugs were used together, there were significant difference. The study using ratio of slope five-point biol. assay also confirmed that the two drugs combination could increase the anti-arrhythmic effects. As shown in the experiment, the anti-arrhythmic effects of two drugs and single drug were all significant compared with that of control group and indicated by many ways that small dose combination group presented synergism.

IT 72063-47-9, Changrolin

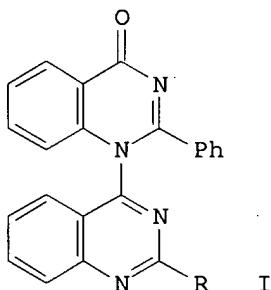
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiarrhythmic activity of cibenzoline and/or)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 117 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1993:517202 HCPLUS
 DOCUMENT NUMBER: 119:117202
 TITLE: Study on the synthesis of some new
 1,4-dihydro-4-oxoquinazoline derivatives
 AUTHOR(S): Gineinah, Magdy M.; Shehata, Ihsan A.; Moustafa,
 Mohamed A.; Abdelal, Ali M.
 CORPORATE SOURCE: Fac. Pharm., Univ. Mansoura, Mansoura, Egypt
 SOURCE: Zhonghua Yaoxue Zazhi (1993), 45(1), 7-14
 CODEN: CYHCEX; ISSN: 1016-1015
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



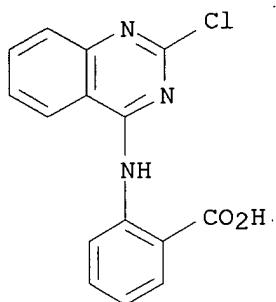
AB Attempts to the synthesis of 1,4-dihydro-4-oxoquinazolines I (R = H, Cl) through different methods are described. New compds. were obtained through these attempts as intermediates, namely, substituted 2-aminobenzoic acids and their corresponding amides.

IT 19589-46-9P

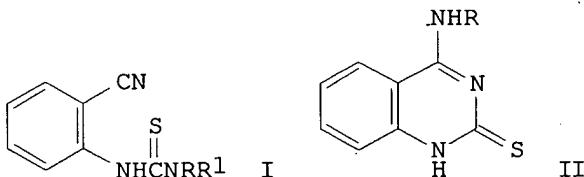
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and amidation of)

RN 19589-46-9 HCPLUS

CN Benzoic acid, 2-[(2-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 118 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1993:233991 HCAPLUS
 DOCUMENT NUMBER: 118:233991
 TITLE: Thermal behavior of some 2-(3-R-thioureido)benzonitriles
 AUTHOR(S): Pazdera, P.; Meindl, J.; Novacek, E.
 CORPORATE SOURCE: Fac. Nat. Sci., Masaryk Univ., Brno, CS-611 37, Czech.
 SOURCE: Chemical Papers (1992), 46(5), 322-8
 CODEN: CHPAEG; ISSN: 0366-6352
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 118:233991
 GI



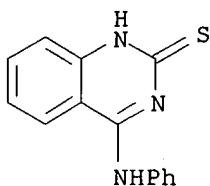
AB The thermal behavior of some 2-(3-organothioureido)benzonitriles, e.g., I ($R = \text{cyclohexyl, PhCH}_2, \text{Ph}$, $R_1 = \text{H}$), above their m.p. without solvent or in boiling aqueous DMF was followed. The primary and secondary alkyl or aryl derivs. afforded cyclization-Dimroth rearrangement products 4-(organoamino)-2-thioxo-1,2-dihydroquinazolines II (same R). Compound I ($R = \text{Me}_3\text{C}$, $R_1 = \text{H}$) eliminated methylpropene and cyclized to 4-amino-2-thioxo-1,2-dihydroquinazoline. 2-(3-Adamantylthioureido)benzonitrile under similar conditions decomposed to amino adamantane and 2-isothiocyanatobenzonitrile. 2-(3,3-Diorganothioureido)benzonitriles I [$R = R_1 = \text{Me, Et, Bu, (CH}_2)_2\text{OH}$, $RR_1 = (\text{CH}_2)_4, (\text{CH}_2)_5, (\text{CH}_2)_2\text{O}(\text{CH}_2)_2$] under similar conditions eliminated alkene followed by cyclization and Dimroth rearrangement to give 4-(organoamino)-2-thioxo-1,2-dihydroquinazolines II [$R = \text{Me, Et, Bu, H, CH}_2\text{CH}_2\text{CH:CH}_2, (\text{CH}_2)_3\text{CH:CH}_2, (\text{CH}_2)_2\text{OCH:CH}_2$, resp.]. Heating 2-(3,3-dimethylthioureido)benzonitrile formed a carbene that either dimerized or polymerized, depending on conditions.

IT 35696-83-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

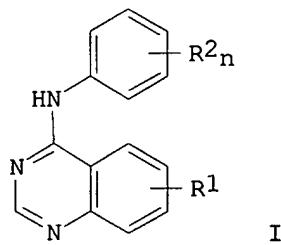
RN 35696-83-4 HCAPLUS

CN 2(1H)-Quinazolinethione, 4-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 119 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1993:191758 HCPLUS
 DOCUMENT NUMBER: 118:191758
 TITLE: Preparation of 4-anilinoquinazolines as neoplasm inhibitors
 INVENTOR(S): Barker, Andrew John; Davies, David Huw
 PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
 SOURCE: Eur. Pat. Appl., 21 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------|--|----------|-----------------|------------|
| EP 520722 | A1 | 19921230 | EP 1992-305703 | 19920622 |
| EP 520722 | B1 | 19961227 | | |
| R: AT, BE, CH, ZA 9204083 | DE, DK, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE A | 19930224 | ZA 1992-4083 | 19920604 |
| CA 2071087 | A1 | 19921229 | CA 1992-2071087 | 19920611 |
| HU 61290 | A2 | 19921228 | HU 1992-1964 | 19920612 |
| IL 102204 | A | 19970318 | IL 1992-102204 | 19920615 |
| AU 9218422 | A | 19930107 | AU 1992-18422 | 19920622 |
| AU 651215 | B2 | 19940714 | | |
| AT 146781 | T | 19970115 | AT 1992-305703 | 19920622 |
| NO 9202517 | A | 19921229 | NO 1992-2517 | 19920625 |
| NO 180105 | B | 19961111 | | |
| NO 180105 | C | 19970219 | | |
| JP 05208911 | A | 19930820 | JP 1992-167416 | 19920625 |
| PRIORITY APPLN. INFO.: | | | GB 1991-13970 | A 19910628 |
| | | | GB 1992-1133 | A 19920120 |
| OTHER SOURCE(S): GI | MARPAT 118:191758 | | | |



AB Title compds. (I; R1 = H, CF3, NO2, halo; R2 = halo, CF3, NO2, alkyl, alkoxy, etc.; n = 1 or 2) were prepared Thus, 3-BrC6H4NH2 was condensed

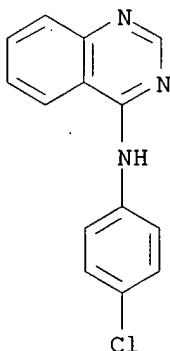
with 4-chloroquinazoline to give I ($R_1 = H$, $R_2 = 3\text{-Br}$, $n = 1$) which had IC₅₀ of 0.02 and 0.78 μM against receptor tyrosine kinase and growth of human nasopharyngcal cell line KB in nitro, resp.

IT 34923-97-2P

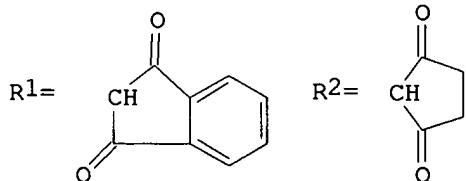
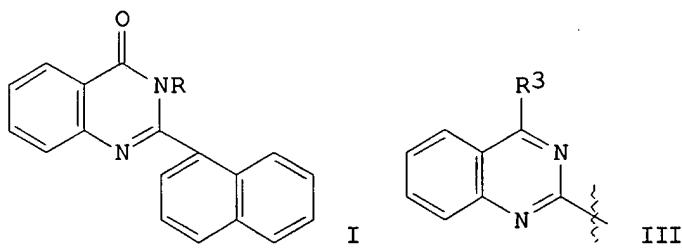
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)

RN 34923-97-2 HCPLUS

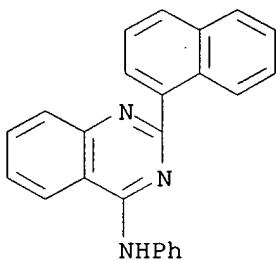
CN 4-Quinazolinamine, N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 120 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1993:124487 HCPLUS
 DOCUMENT NUMBER: 118:124487
 TITLE: Synthesis and reactions of 2-(α -naphthyl)-4-(3H)-quinazolinone
 AUTHOR(S): El-Farargy, A. F.; Hamad, M. M.; Said, S. A.; Haikal, A.
 CORPORATE SOURCE: Fac. Sci., Zagazig Univ., Zagazig, Egypt
 SOURCE: Egyptian Journal of Chemistry (1991), Volume Date 1990, 33(3), 283-9
 CODEN: EGJCA3; ISSN: 0367-0422
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 118:124487
 GI



- AB Quinazolinone I ($R = H$) was prepared via fusion of formamide with 2-(α -naphthyl)-3,1-(4H)-benzoxazin-4-one. I was treated with MeI in BuOH to give I ($R = Me$), which underwent fusion with phthalimide or succinic anhydride to give I ($R = R_1, R_2$), resp. Condensation of I ($R = Me$) with PhCHO or 4-MeOC₆H₄CHO gave I ($R = CH:CHPh, CH:CHC_6H_4OMe-4$), resp. Chlorination of I ($R = H$) gave chloride II ($R_3 = Cl$) which was treated with PhNH₂, NH₂NH₂, or NaN₃ to give II ($R_3 = NPh, NNH_2, N_3$), resp. Alkylation of I ($R = H$) with Me₂SO₄ or ClCH₂CO₂Et gave ether II ($R_3 = OMe, OCH_2CO_2Et$), resp. Further treatment of II ($R_3 = OCH_2CO_2Et$) with amines gave amides II ($R_3 = OCH_2CONHR_4, R_4 = NH_2, NPh, Ph, C_6H_4Me-4$).
- IT 133594-93-1P, 4-Anilino-2-(1-naphthyl)quinazoline
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
- RN 133594-93-1 HCPLUS
- CN 4-Quinazolinamine, 2-(1-naphthalenyl)-N-phenyl- (9CI) (CA INDEX NAME)

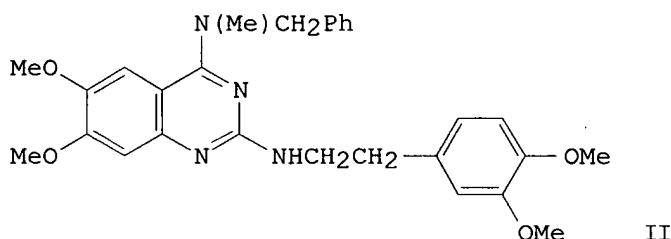
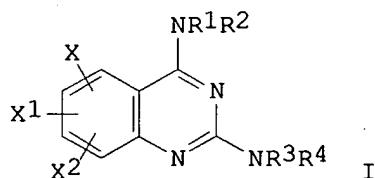


L6 ANSWER 121 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:651366 HCPLUS
 DOCUMENT NUMBER: 117:251366
 TITLE: Preparation of 2,4-diaminoquinazoline derivatives for enhancing antitumor activity
 INVENTOR(S): Coe, Jotham W.; Fliri, Anton F. J.; Kaneko, Takushi; Larson, Eric R.
 PATENT ASSIGNEE(S): Pfizer Inc., USA
 SOURCE: PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9214716 | A1 | 19920903 | WO 1992-US28 | 19920108 |
| W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, SU, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| CA 2101542 | A1 | 19920821 | CA 1992-2101542 | 19920108 |
| AU 9211848 | A | 19920915 | AU 1992-11848 | 19920108 |
| AU 655798 | B2 | 19950112 | | |
| EP 572437 | A1 | 19931208 | EP 1992-903632 | 19920108 |
| EP 572437 | B1 | 19950426 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 06500117 | T | 19940106 | JP 1992-503777 | 19920108 |
| HU 64755 | A2 | 19940228 | HU 1993-2384 | 19920108 |
| BR 9205645 | A | 19940607 | BR 1992-5645 | 19920108 |
| AT 121735 | T | 19950515 | AT 1992-903632 | 19920108 |

| | | | | |
|------------------------|----|----------|----------------|------------|
| ES 2071484 | T3 | 19950616 | ES 1992-903632 | 19920108 |
| CN 1064271 | A | 19920909 | CN 1992-101113 | 19920219 |
| ZA 9201911 | A | 19930819 | ZA 1992-1191 | 19920219 |
| NO 9302954 | A | 19930819 | NO 1993-2954 | 19930819 |
| PRIORITY APPLN. INFO.: | | | US 1991-657922 | A 19910220 |
| | | | WO 1992-US28 | A 19920108 |

GI

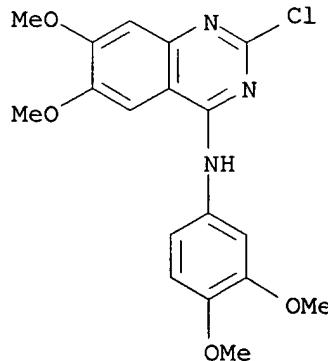


AB Title compds. [I; X = alkyl, alkoxy, Cl, F, (di)(alkyl)amino, CF₃; X₁ = H, alkyl, F, Cl, dialkylamino; X₂ = H, alkyl; XX₁ = OCH₂O, OCH₂CH₂O; R₁ = H, alkyl; R₂ = alkyl, (substituted) aralkyl; R₃ = H, alkyl; R₄ = (substituted) aralkyl], was prepared as potentiators of neoplasm inhibitors (no details). Thus, 2,4-dichloro-6,7-dimethoxyquinazoline, N-methylbenzylamine, and Et₃N were stirred 5 h to give 2-chloro-4-(N-methylbenzylamino)-6,7-dimethylquinazoline. The latter was heated with 3,4-dimethoxyphenethylamine and EtN(CHMe₂)₂ in EtOCH₂CH₂OCH₂CH₂OH to give title compound II.

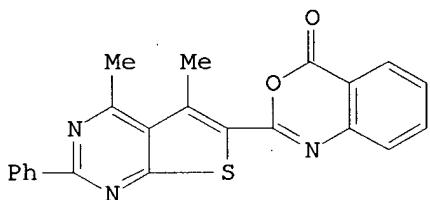
IT 144511-78-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for neoplasm inhibitor potentiator)

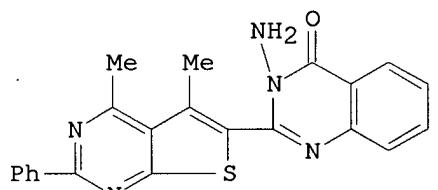
RN 144511-78-4 HCAPLUS

CN 4-Quinazolinamine, 2-chloro-N-(3,4-dimethoxyphenyl)-6,7-dimethoxy- (9CI)
(CA INDEX NAME)

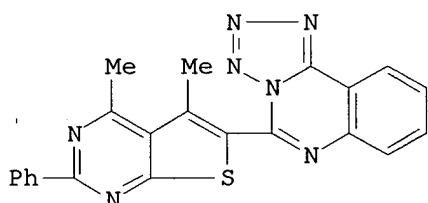
L6 ANSWER 122 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:651324 HCPLUS
 DOCUMENT NUMBER: 117:251324
 TITLE: Some reactions with 4-carboxymethylthio-2-phenyl-5-acetylpyrimidine
 AUTHOR(S): El-Bahaie, S.; Bayoumy, B. E.; Assy, M. G.;
 El-Kafrawy, A.; Yousif, Sh.
 CORPORATE SOURCE: Fac. Sci., Zagazig Univ., Zagazig, Egypt
 SOURCE: Egyptian Journal of Pharmaceutical Sciences (1991),
 32(1-2), 415-20
 DOCUMENT TYPE: CODEN: EJPSBZ; ISSN: 0301-5068
 LANGUAGE: Journal
 OTHER SOURCE(S): English
 GI: CASREACT 117:251324



I



II



III

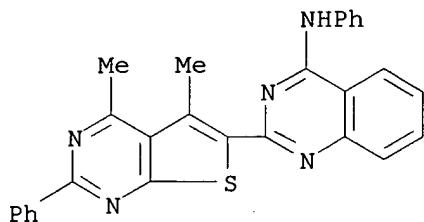
AB (Thienopyrimidinyl)benzoxazinone I was prepared Hydrazinolysis of I gave the (thienopyrimidinyl)quinazolinone II. The tetrazoloquinazolinylthieny[2,3-d]pyrimidine III was also prepared

IT 139436-19-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 139436-19-4 HCPLUS

CN 4-Quinazolinamine, 2-(4,5-dimethyl-2-phenylthieno[2,3-d]pyrimidin-6-yl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 123 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:633965 HCAPLUS

DOCUMENT NUMBER: 117:233965

TITLE: Synthesis and antihypertensive activity of
1,4-disubstituted piperazinesAUTHOR(S): Abou-Zeid, K. A. M.; Youssef, K. M.; Amine, F. M.;
Botros, S.

CORPORATE SOURCE: Fac. Pharm., Cairo Univ., Cairo, Egypt

SOURCE: Egyptian Journal of Pharmaceutical Sciences (1991),
32(1-2), 165-74

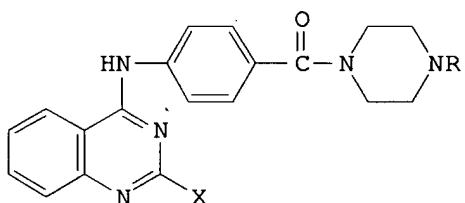
CODEN: EJPSBZ; ISSN: 0301-5068

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 117:233965

GI



II

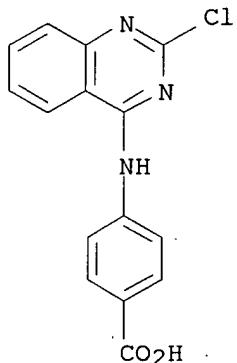
AB The synthesis of a new series of 1-aryl-4-[4(4-quinazolinylamino)benzoyl]piperazines was achieved. 2,4-Dichloroquinazoline was reacted with p-aminobenzoic acid to afford the key compound 2-chloro-4-(4-carboxyanilino)quinazoline (I), which was converted to the corresponding acid chloride with thionyl chloride followed by treatment with arylpiperazines to give the intermediate II ($X = Cl$). The latter was reacted with cyclic amines to yield the target compds. II ($X = NR_2$). In an alternative synthesis of II ($X = NR_2$), intermediate I was first reacted with cyclic amines to give 2-amino-4-(4-carboxyanilino)quinazoline (III). Reaction of III with 1-arylpiperazines afforded the desired compds. II ($X = NR_2$). The synthesized compds. showed no hypotensive activity as tested in anesthetized normotensive rabbits.

IT 144259-34-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with cyclic secondary amines)

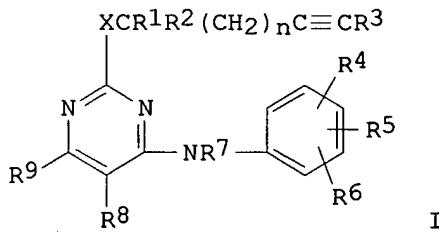
RN 144259-34-7 HCAPLUS

CN Benzoic acid, 4-[(2-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 124 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:255629 HCAPLUS
 DOCUMENT NUMBER: 116:255629
 TITLE: Preparation of 4-anilinopyrimidines as agrochemical fungicides
 INVENTOR(S): Minn, Klemens; Braun, Peter; Sachse, Burkhard; Wicke, Heinrich
 PATENT ASSIGNEE(S): Hoechst A.-G., Germany
 SOURCE: Ger. Offen., 54 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|--------|------------|-----------------|------------|
| DE 4029648 | A1 | 19920326 | DE 1990-4029648 | 19900919 |
| ZA 9107428 | A | 19920429 | ZA 1991-7428 | 19910918 |
| WO 9205158 | A1 | 19920402 | WO 1991-EP1791 | 19910919 |
| W: BR, CA, CS, FI, NO, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| PRIORITY APPLN. INFO.: | | | DE 1990-4029648 | A 19900919 |
| OTHER SOURCE(S): | MARPAT | 116:255629 | | |
| GI | | | | |



AB Title compds. I [R1, R2 = H, C1-9 alkyl, substituted C1-4 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-9 cycloalkyl, etc. or R1R2 = 4-10 membered (hetero)cyclic ring; R3 = H, halo, (substituted) C1-4 alkyl, C1-4 alkylthio, etc.; R4-R6 = H, halo, OH, NH2, NO2, cyano, C1-4 alkyl, etc. or 2 of R4-R6 = 4-10 membered (hetero)cyclic ring; R7 = H, CHO, (substituted) C1-4 alkyl, -C1-4 alkoxy, -amino, etc.; R8, R9 = H, halo, (substituted)

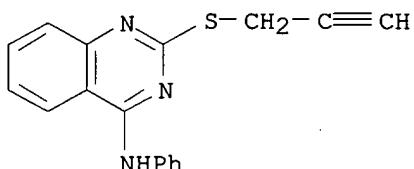
C1-4 alkyl, -C1-4 alkoxy, -C1-4 alkylthio, etc. or R8R9 = 4-10 membered (hetero)cyclic ring; X = O, S; n = 0-8] were prepared as agrochem. fungicides. Thus, HCO₂Et, MeOCH₂CO₂Me and thiourea were cyclocondensed to give 5-methoxy-2-mercaptop-1,3-dihydropyrimidin-4-one. This was S-alkylated by BrCH₂C.tpbond.CH and the product was converted to the 4-chloro derivative by POC₁3. This was treated with aniline to give I (R1-R7 = H; R8 = OMe; R9 = H; X = S; n = 0) (II). II at 60 ppm gave complete control of *Pseudocercospora* herbotrichoides on wheat.

IT 141598-82-5P

RL: PREP (Preparation)
(prepare of, as agrochem. fungicide)

RN 141598-82-5 HCPLUS

CN 4-Quinazolinamine, N-phenyl-2-(2-propynylthio)- (9CI) (CA INDEX NAME)



L6 ANSWER 125 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:214451 HCPLUS

DOCUMENT NUMBER: 116:214451

TITLE: Cyclic amidines. Part 27. An unambiguous synthesis
of 5,10,14c-triazabenzo[a]naphth[1,2,3-de]anthracene
by a palladium-catalyzed cyclodehalogenation

AUTHOR(S): Upton, Christopher

CORPORATE SOURCE: Sch. Pharm. Pharmacol., Univ. Bath, Bath, BA2 7AY, UK

SOURCE: Journal of Chemical Research, Synopses (1992), (4),

119

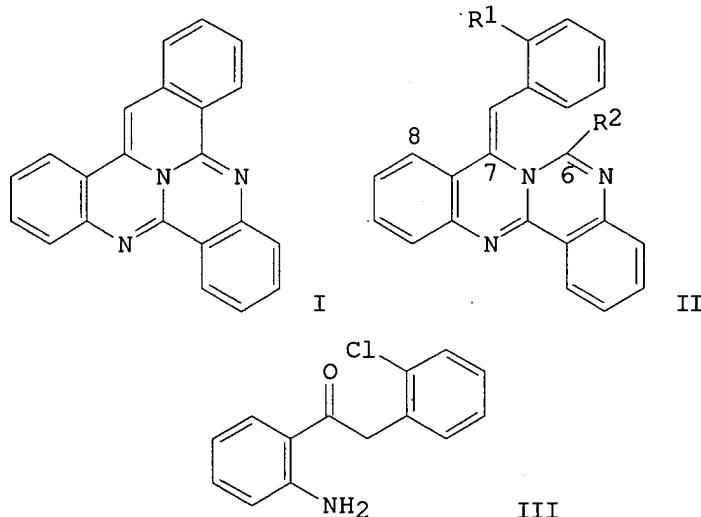
CODEN: JRPSDC; ISSN: 0308-2342

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 116:214451

GI



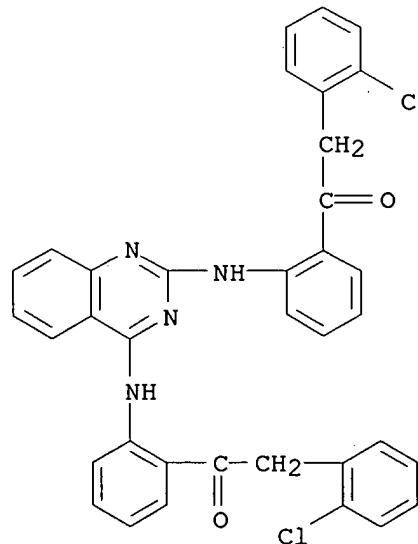
AB An unambiguous route to the title triazabenzonaphthanthracene (I) is reported via a palladium-catalyzed cyclocondensation of the 6-chloro-7-(2-chlorobenzylidene)benzanthracene II ($R_1 = R_2 = Cl$) avoiding high temperature reactions and the possibility of skeletal rearrangement. The aminophenyl benzyl ketone III, was obtained by ozonolysis of 3-(2-chlorobenzyl)-2-methylindole and is converted in a stepwise manner to the triazabenzonaphthanthracene I.

IT 141034-47-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 141034-47-1 HCPLUS

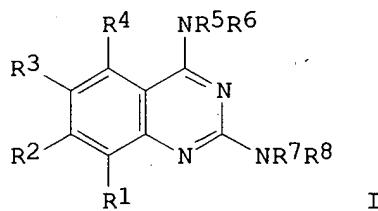
CN Ethanone, 1,1'-[2,4-quinazolinediylbis(imino-2,1-phenylene)]bis[2-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 116:174164
 TITLE: Preparation of diaminoquinazoline derivatives as ulcer inhibitors
 INVENTOR(S): Ife, Robert J.; Brown, Thomas H.; Leach, Colin A.; Keeling, David J.
 PATENT ASSIGNEE(S): SmithKline Beecham Intercredit B. V., UK
 SOURCE: U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 467,075, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5064833 | A | 19911112 | US 1990-520561 | 19900508 |
| ZA 9003479 | A | 19911224 | ZA 1990-3479 | 19900508 |
| PRIORITY APPLN. INFO.: | | | US 1988-278064 | B2 19881130 |
| | | | GB 1989-10722 | A 19890510 |
| | | | US 1990-467075 | B2 19900118 |

OTHER SOURCE(S): MARPAT 116:174164
 GI



AB Substituted diaminoquinazoline derivs. (I: R1- R4 = H, C1-4 alkyl, C1-4 alkoxy, Ph, C1-4 alkylthio, etc.; R5, R6 = H, C1-4 alkyl; NR5R6 = piperidino, morpholino, imidazolyl, pyridyl, pyrrolidine ring; R7, R8 = H, C1-4; NR7R8 with N = piperidino, morpholino, imidazolyl, pyridyl, pyrrolidine ring) are inhibitors of H+/K+ATPase enzyme and useful for the inhibition of increased gastric acid secretion. Thus, 8-methoxy-4-(2-methylphenylamino)-2-chloroquinazoline (preparation given) was heated with ethanolic ammonia for 3 h to obtain 2-amino-4-(2-methylphenylamino)-8-methoxyquinazoline (II). II at 10 µmol/kg inhibited pentagastrin-stimulated gastric acid secretion in rats by 60%. A tablet contained II 100, lactose 153, starch 33, crospovidone 12, microcryst. cellulose 30, Mg stearate 2 mg.

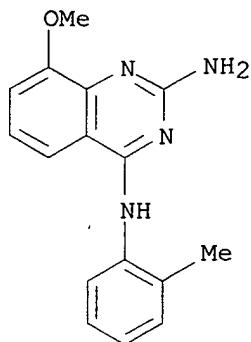
IT 124309-23-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of diaminoquinazoline derivative as

ulcer inhibitor)

RN 124309-23-5 HCAPLUS

CN 2,4-Quinazolinediamine, 8-methoxy-N4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 127 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:151703 HCPLUS

DOCUMENT NUMBER: 116:151703

TITLE: Reactions with 4-carboxymethylthio-2-phenyl-5-acetylpyrimidine

AUTHOR(S): El-Bahaie, Said; Bayoumy, Basher E.; Assy, M. G.; Yousif, S.

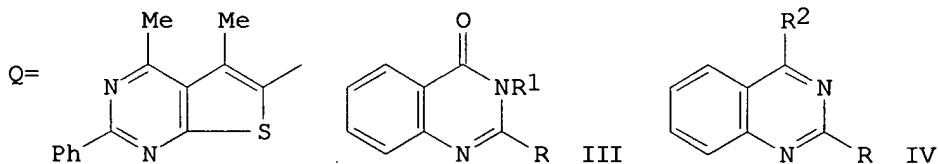
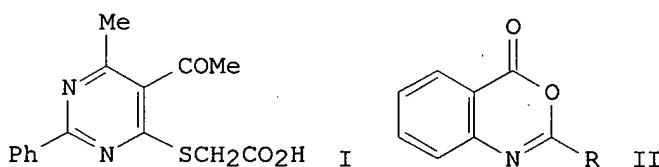
CORPORATE SOURCE: Fac. Sci., Zagazig Univ., Zagazig, Egypt

SOURCE: Polish Journal of Chemistry (1991), 65(5-6), 1059-64
CODEN: PJCHDQ; ISSN: 0137-5083

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



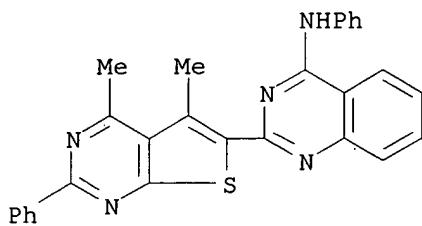
AB Treating the title compound I sequentially with SOCl_2 , $2-\text{H}_2\text{NC}_6\text{H}_4\text{CO}_2\text{H}$ in AcOH , and Ac_2O gave oxobenzoxazinylthienopyrimidine II ($R = Q$). Cyclocondensation of II with aromatic amines, hydrazines, NH_3 and glycine gave quinazolines III ($R_1 = \text{Ph}, \text{C}_6\text{H}_4\text{Br}-4, \text{C}_6\text{H}_4\text{OMe}-4, \text{NH}_2, \text{NHPH}, \text{CH}_2\text{CO}_2\text{H}, \text{H}$). Chlorination of III ($R_1 = \text{H}$) with $\text{PCl}_5-\text{POCl}_3$ led to a number of quinazolinylthienopyrimidine derivs., e.g., IV ($R_2 = \text{NHPH}, \text{NHNHPh}, \text{NHN:CHPh}, \text{NHNHCOC}_6\text{H}_4\text{Cl}-4$), via substitution of IV ($R_2 = \text{Cl}$) and in some cases condensation with aldehydes or acylation with acid chlorides.

IT 139436-19-4P

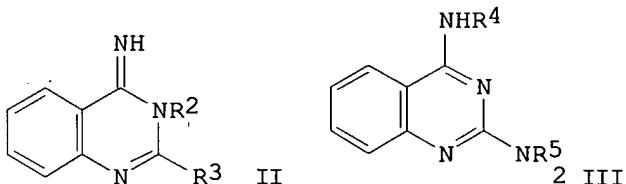
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 139436-19-4 HCPLUS

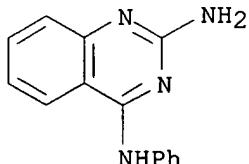
CN 4-Quinazolinamine, 2-(4,5-dimethyl-2-phenylthieno[2,3-d]pyrimidin-6-yl)-N-phenyl- (9CI) (CA INDEX NAME)



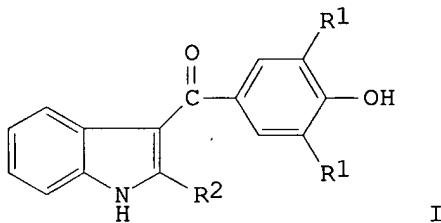
L6 ANSWER 128 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:59312 HCAPLUS
 DOCUMENT NUMBER: 116:59312
 TITLE: 2-(3-Acylthioureido)benzonitriles. II. Synthesis of N-substituted 2,4-diaminoquinazolines
 AUTHOR(S): Pazdera, P.; Potucek, V.
 CORPORATE SOURCE: Fac. Nat. Sci., Masaryk Univ., Brno, CS-611 37, Czech.
 SOURCE: Chemical Papers (1991), 45(5), 677-86
 CODEN: CHPAEG; ISSN: 0366-6352
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Desulfuration of 2-NCC₆H₄NHCSNHCOR (R = Me, OEt, Ph) with HgO in the presence of R₁NH₂ (R₁ = Ph, Et) and NEt₂ in acetone at room temperature gave 2-NCC₆H₄NHC(NHCOR):NR₁ (I) and 2-NCC₆H₄NHC(NEt₂):NCOR, resp., or the products of their cyclization, (acylamino)iminoquinazolines II (R₂ = R₁, R₃ = NHCOR; R₂ = COR, R₃ = NEt₂, resp.) and quinazolines III (R₄ = COR, R₅ = Et). I and II (R₂ = R₁, R₃ = NHCOR) underwent base-catalyzed rearrangement with simultaneous hydrolysis of the acyl group to give III (R₄ = Ph, Et, R₅ = H).
 IT 138493-40-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 138493-40-0 HCAPLUS
 CN 2,4-Quinazolinediamine, N4-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 129 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:622783 HCPLUS
 DOCUMENT NUMBER: 115:222783
 TITLE: Anti-arrhythmic activities of six indole derivatives
 of changrolin
 AUTHOR(S): Dai, Dezai; Rong, Pei; Huang, Jun; Liu, Jie; Cheng,
 Jianhua; Chen, Yunhai; Qiu, Yitang; Huang, Wenlong;
 Peng, Sixun
 CORPORATE SOURCE: Res. Div. Pharmacol., China Pharm. Univ., Nanjing,
 210009, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1991), 12(5), 411-15
 CODEN: CYLPDN; ISSN: 0253-9756
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



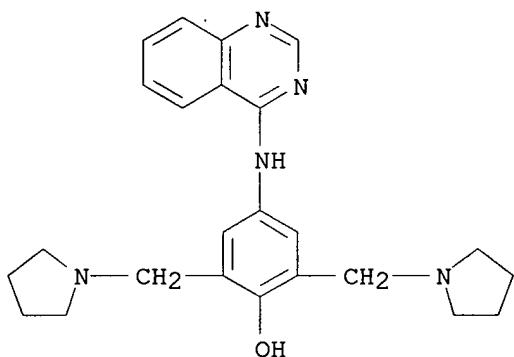
AB The indole-derived compds. I ($R_1 = \text{piperidino, pyrrolidinyl, morpholino}$; $R_2 = \text{Me, Ph}$), which possessed side chains resembling changrolin (II), showed potent antiarrhythmic activity by restoration of sinus rhythm from ouabain-induced tachycardia in guinea pigs. The potency was assessed by comparison of the maintenance time of sinus rhythm recovered from tachyarrhythmias induced by ouabain. The promising compound is I ($R_1 = \text{piperidino}$; $R_2 = \text{Me}$) (III). There was no difference in antiarrhythmic activities resulting from substitutions between a benzene ring and Me residue at position 2 of indole, but the latter had weaker parasympatholytic activity. The antiarrhythmic activity of III (>60 min) was 2.4 times more potent than II (25 min), but its anticholinergic activity was only half of the latter. Suppressive effect on reperfusion-induced arrhythmias by i.v. III was compared at different times in relation to the ligation-reperfusion protocol; it was the most effective when administered either 30 min prior to coronary occlusion or at the moment of reperfusion. I might belong to the Ic group as shown by the slowing of impulse conduction within the heart.

IT 72063-47-9, Changrolin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiarrhythmic activity of, anticholinergic activity and structure in relation to)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 130 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:526390 HCAPLUS

DOCUMENT NUMBER: 115:126390

TITLE: Spatial requirements of the sodium channel binding site for class I antiarrhythmics as derived from the crystal structures of 4-substituted 2,6-bis(1-pyrrolidinylmethyl)phenols

AUTHOR(S): Glowka, Marek L.; Dargie, Robin L.; Codding, Penelope W.

CORPORATE SOURCE: Dep. Chem., Univ. Calgary, Calgary, AB, T2N 1N4, Can.
SOURCE: Journal of Medicinal Chemistry (1991), 34(9), 2678-84

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

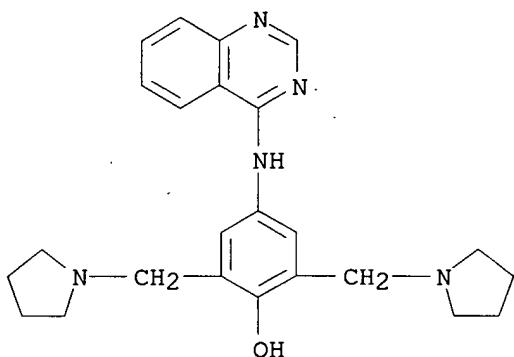
AB The mol. structures of 4 class I antiarrhythmic agents containing a bis(1-pyrrolidinylmethyl)phenol framework were determined by x-ray diffraction methods and their conformations were analyzed by mol. mechanics. Each structure has an intramol. H bond between the phenol OH group and one pyrrolidine N atom; this bond dets. the orientation of the pyrrolidine ring. Only 2 distinct orientations are observed for the other pyrrolidine ring; the combination of the pyrrolidine ring positions produces mol. conformers that either have the 2N atoms on the same side of the phenol ring plane or have the N atoms nearly coplanar with the phenol ring. Crystallog. conformations of benzamides as well as those calculated with mol. mechanics find a preferred conformation that has the 3 planar regions tilted by ca. 30° with respect to one another. The combined restrictions of the H bond, the conformational preferences for the bis(pyrrolidinylmethyl)phenol moiety, and a consistent conformation for the central benzamide portion provide a suggestion of the active shape of class Ic antiarrhythmic drugs. The distance between 2 potential recognition groups-a Ph ring' (lipophilic group) separated by 3.8 Å from an O atom and a secondary or tertiary amine-is unique for class Ic antiarrhythmics as compared to other class I antiarrhythmics, such as lidocaine, quinidine, procainamide and disopyramide, and suggests a correlation between the mol. structures and the activity of class I antiarrhythmics.

IT 72063-47-9

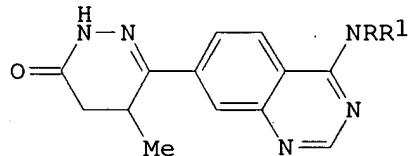
RL: BIOL (Biological study)
(antiarrhythmic activity and crystal structure of)

RN 72063-47-9 HCAPLUS

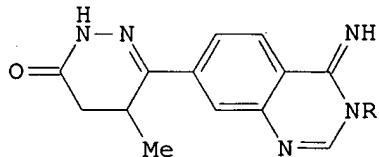
CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 131 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:505445 HCAPLUS
 DOCUMENT NUMBER: 115:105445
 TITLE: Studies on cardiotonic agents. VII. Potent cardiotonic agent KF15232 with myofibrillar calcium sensitizing effect
 AUTHOR(S): Nomoto, Yuji; Takai, Haruki; Ohno, Tetsuji; Kubo, Kazuhiro
 CORPORATE SOURCE: Pharm. Res. Lab., Fuji, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(4), 900-10
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I, R=H, alkyl, cycloalkyl, etc., R¹=H, RR¹=alkylene

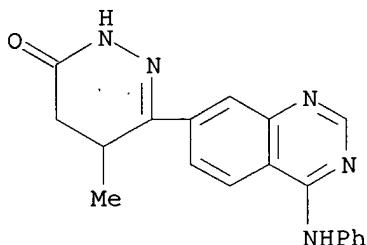


II, R=NH₂, alkyl, Ph, etc.

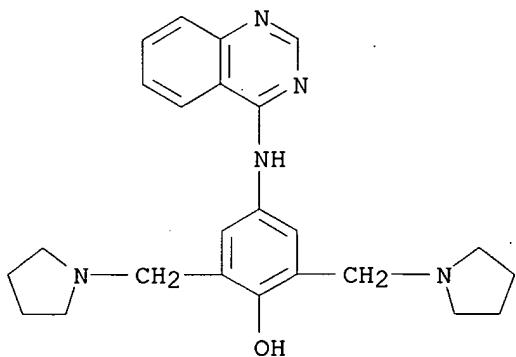
AB A series of novel 4,5-dihydro-5-methyl-6-(4-substituted 7-quinazolinyl)-3-(2H)pyridazinones (I) was synthesized and examined for cardiotonic activity in anesthetized dogs. The 4-substituted aminoquinazolines generally showed potent and long-lasting inotropic activity. Fall in the activity was observed on the introduction of substituent at the 2-position of the quinazoline ring. The 3-substituted 4-(3H)quinazolinimines (II) generally exhibited weak activity. Ca²⁺

sensitizing effect of the 4-substituted amino derivs. was also examined in chemical skinned fiber from papillary muscle of guinea pig. The alkylamine derivs. exhibited small sensitizing effect, while the benzylamino derivs. exhibited large effect. Among them, KF15232 (Ix) was found to have the most potent cardiotonic and Ca²⁺ sensitizing activities.

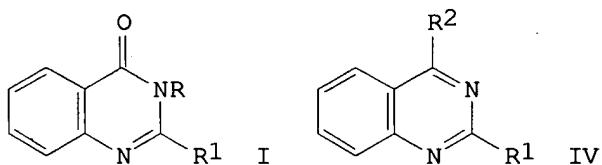
IT 124294-54-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and cardiotonic activity of, structure in relation to)
 RN 124294-54-8 HCAPLUS
 CN 3(2H)-Pyridazinone, 4,5-dihydro-5-methyl-6-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 132 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:485122 HCAPLUS
 DOCUMENT NUMBER: 115:85122
 TITLE: Modeling and kinetic analysis on changrolin block of cardiac sodium channels
 AUTHOR(S): Wu, Yuejin; Fang, Dachao
 CORPORATE SOURCE: Dep. Pharmacol., Tongji Med. Univ., Wuhan, 430030, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1991), 12(4), 363-7
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB Modeling and kinetic anal. on changrolin (CRL) blockade of cardiac Na⁺ channels based on the model of gate-related receptor hypothesis were performed by computer simulation. A simple procedure suitable for analyzing steady-state blocking data was developed. CRL blocks activated Na⁺ channels, and with the onset rate of 0.0347 AP-1 at driving rate of 1.0 Hz. The time constant of recovery from block at resting potential of -81 mV was 43.29 s and increased with hyperpolarization, suggesting that CRL may be trapped in channel by activation gate. The studies also showed no shift on the h_∞ curve in the presence of CRL. These results suggest that the binding site of CRL in Na⁺ channel is activation gate-related receptor site.
 IT 72063-47-9, Changrolin
 RL: BIOL (Biological study)
 (heart sodium channel blockade by, modeling and kinetic anal. of, computer simulation in)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 133 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:207187 HCAPLUS
 DOCUMENT NUMBER: 114:207187
 TITLE: Synthesis and reaction of 2-(α -naphthyl)-4-(3H)-quinazolinone
 AUTHOR(S): El-Farargy, A. F.; Hamad, M. M.; Said, S. A.; Haikal, A.
 CORPORATE SOURCE: Fac. Sci., Zaggazig Univ., Zagazig, Egypt
 SOURCE: Anales de Quimica (1990), 86(7), 782-5
 CODEN: ANQUEX; ISSN: 1130-2283
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 114:207187
 GI

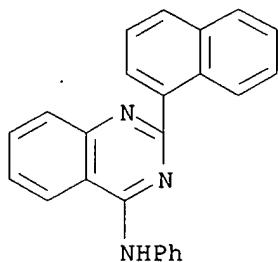


AB Reaction of 2-(1-naphthyl)-3,1-[4H]benzoxazin-4-one with formamide in dry xylene gave 2-(1-naphthyl)quinazolinone I ($R = H$, 1-naphthyl (II)). II reacted with Me iodide, $POCl_3/PCl_5$, Et chloroacetate or di-Me sulfate to give I ($R = Me$, $R_1 = 1$ -naphthyl) (III) and IV ($R_1 = 1$ -naphthyl, $R_2 = Cl$, OCH_2CO_2Et , OMe) resp. The condensation of III with benzaldehyde or p-anisaldehyde gave styryl derivs. I ($R = CH:CHR_3$; $R_3 = Ph$, C_6H_4OMe-4). Treatment of IV ($R_2 = OCH_2CO_2Et$ with hydrazine, Ph hydrazine, aniline and p-toluidine gave the corresponding amides IV ($R_2 = OCH_2CONHR_4$; $R_4 = NH_2$, $NHPh$, Ph , C_6H_4Me-4) resp.

IT 133594-93-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 133594-93-1 HCAPLUS

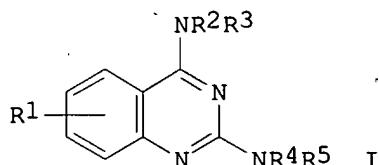
CN 4-Quinazolinamine, 2-(1-naphthalenyl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 134 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:185535 HCAPLUS
 DOCUMENT NUMBER: 114:185535
 TITLE: Preparation of quinazoline derivatives as inhibitors of gastric acid secretion
 INVENTOR(S): Brown, Thomas Henry; Ife, Robert John; Leach, Colin Andrew; Keeling, David John
 PATENT ASSIGNEE(S): SmithKline Beecham Intercredit B. V., Neth.
 SOURCE: Eur. Pat. Appl., 18 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------|--------------------|----------------------------|-----------------|------------|
| EP 404322 | A1 | 19901227 | EP 1990-304979 | 19900509 |
| EP 404322 | B1 | 19930922 | | |
| R: AT, BE, CH, CA 2015981 | DE, DK, ES, FR, A1 | GB, GR, IT, LI, LU, NL, SE | | |
| ZA 9003479 | | CA 1990-2015981 | 19900503 | |
| AU 9054864 | A | 19911224 | ZA 1990-3479 | 19900508 |
| AU 627576 | A | 19901115 | AU 1990-54864 | 19900509 |
| AT 94875 | B2 | 19920827 | | |
| JP 03017068 | T | 19931015 | AT 1990-304979 | 19900509 |
| | A | 19910125 | JP 1990-121063 | 19900510 |
| PRIORITY APPLN. INFO.: | | | GB 1989-10722 | A 19890510 |
| | | | GB 1989-18703 | A 19890816 |
| | | | GB 1989-28251 | A 19891214 |
| | | | EP 1990-304979 | A 19900509 |

OTHER SOURCE(S): MARPAT 114:185535
 GI



AB The title compds. [I; R₁ = OH, hydroxyalkyl, hydroxyalkoxy, carboxyalkoxy, alkoxyalkoxy, (ring-substituted) heterocycl-l-n-alkyl, (N-substituted) aminoalkyl or amino-n-alkoxy; R₂-R₄ = H, alkyl, (ring-substituted) Ph or phenyl-n-alkyl; or NR₂R₃, NR₄R₅ = (un)saturated heterocycl containing ≥1 heteroatoms], useful for treatment of, e.g., gastric and duodenal ulcers,

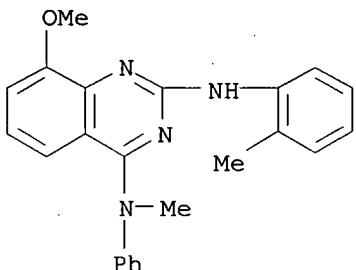
Zollinger-Ellison syndrome, and gastritis, are prepared. Thus, treatment of I ($R_1 = 8\text{-OH}$, $R_2 = \text{o-MeC}_6\text{H}_4$, $R_3 = \text{H}$, $R_4 = \text{Me}$, $R_5 = \text{Ph}$) with NaH in DMF followed by reaction with $\text{BrCH}_2\text{CO}_2\text{Et}$ gave I ($R_1 = 8\text{-OCH}_2\text{CO}_2\text{Et}$; $R_2\text{-}R_5 = \text{same as above}$) which was reduced with LiAlH_4 in THF to give I ($R_1 = 8\text{-OCH}_2\text{CH}_2\text{OH}$, $R_2\text{-}R_5 = \text{same as above}$). A total of 13 I were prepared and in vitro inhibited $\text{H}^+\text{-K}^+$ ATPase activity with IC_{50} of $0.018\text{-}1.3 \mu\text{M}$. I. HCl ($R_1 = 6\text{-OH}$, $R_2 = \text{Me}$, $R_3 = \text{Ph}$, $R_4 = \text{H}$, $R_5 = 2,4\text{-MeFC}_6\text{H}_3$) at $10 \mu\text{M}$ in vitro showed $7 \pm 4\%$ bone resorption by rat osteoclasts sedimented on cortical bone slices vs. $100 \pm 27\%$ (control).

IT 124309-45-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation of)

RN 124309-45-1 HCPLUS

CN 2,4-Quinazolinediamine, 8-methoxy-N⁴-methyl-N²-(2-methylphenyl)-N⁴-phenyl-
(9CI) (CA INDEX NAME)



L6 ANSWER 135 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:164274 HCPLUS

DOCUMENT NUMBER: 114:164274

TITLE: Preparation of 4-(substituted amino)-pyrimidinium salts as cardiovascular agents

INVENTOR(S): Hargreaves, Rodney Brian; Marshall, Paul William; McLoughlin, Bernard Joseph; Mills, Stuart Dennett

PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Brit. UK Pat. Appl., 77 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

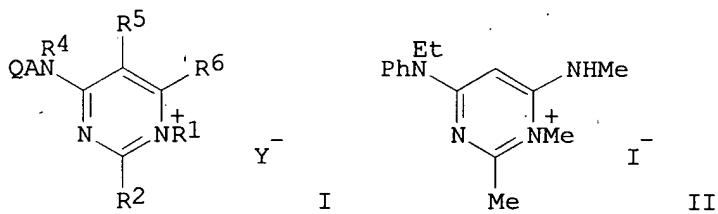
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| GB 2230527 | A | 19901024 | GB 1990-7964 | 19900409 |
| GB 2230527 | B | 19930505 | | |
| ZA 9002753 | A | 19901228 | ZA 1990-2753 | 19900410 |
| IL 94062 | A | 19951127 | IL 1990-94062 | 19900411 |
| CA 2014457 | A1 | 19901021 | CA 1990-2014457 | 19900412 |
| CA 2014457 | C | 19990928 | | |
| WO 9012790 | A1 | 19901101 | WO 1990-GB595 | 19900419 |
| W: AU, BB, BG, FI, HU, JP, KR, LK, MC, MW, NO, RO, SD, SU | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE | | | | |
| AU 9054354 | A | 19901116 | AU 1990-54354 | 19900419 |
| AU 635260 | B2 | 19930318 | | |
| EP 422178 | A1 | 19910417 | EP 1990-906289 | 19900419 |
| EP 422178 | B1 | 19941005 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |

| | | | | |
|------------------------|----|----------|-----------------|------------|
| HU 56080 | A2 | 19910729 | HU 1990-3555 | 19900419 |
| HU 209586 | B | 19940829 | | |
| JP 03505741 | T | 19911212 | JP 1990-506034 | 19900419 |
| JP 2528218 | B2 | 19960828 | | |
| DD 297406 | A5 | 19920109 | DD 1990-339897 | 19900419 |
| ES 2064727 | T3 | 19950201 | ES 1990-906289 | 19900419 |
| RU 2108329 | C1 | 19980410 | RU 1990-4894489 | 19900419 |
| US 5223505 | A | 19930629 | US 1990-513304 | 19900420 |
| PL 165502 | B1 | 19941230 | PL 1990-284871 | 19900420 |
| PL 165917 | B1 | 19950331 | PL 1990-301231 | 19900420 |
| CN 1047080 | A | 19901121 | CN 1990-103931 | 19900421 |
| CN 1024793 | B | 19940601 | | |
| BR 9005295 | A | 19920421 | BR 1990-5295 | 19901019 |
| NO 9005519 | A | 19910220 | NO 1990-5519 | 19901220 |
| NO 177054 | B | 19950403 | | |
| FI 95377 | B | 19951013 | FI 1990-6307 | 19901220 |
| FI 95377 | C | 19960125 | | |
| PRIORITY APPLN. INFO.: | | | GB 1989-9054 | A 19890421 |
| | | | GB 1989-10548 | A 19890508 |
| | | | WO 1990-GB595 | A 19900419 |

OTHER SOURCE(S) : MARPAT 114:164274

GI



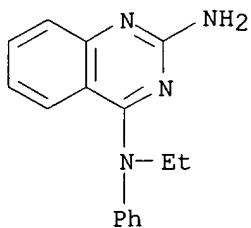
AB The title compds. [I; R1 = alkyl, alkenyl, cycloalkyl(alkyl), phenyl(alkyl), 1 of R2, R6 = amino, pyrrolidino, piperidino, morpholino, the other = H, (alkoxy)alkyl, phenyl(alkyl), cycloalkyl(alkyl), alkenyl; R4 = H, cycloalkylalkyl, alkyl, alkenyl, alkynyl, phenylalkyl; or R4 = (substituted) alkylene or alkenylene bound to QA; R5 = H, alkyl, alkenyl; R5R6 = alkylene, atoms to complete a benzene ring; A = bond, (oxy)alkylene; Q = pyridyl, furyl, thieryl, Ph; Y = physiol. acceptable cation], were prepared Thus, a mixture of 4-chloro-2-methyl-6-methylaminopyrimidine and PhNHET were heated at 160° for 3 h to give 2-methyl-6-methylamino-4-N-ethylanilinopyrimidine.HCl. The free base of the latter was refluxed with MeI in dioxane to give title compound II which in rats had an ED30 of 0.3 mg/kg i.v. for bradycardic activity.

IT 133062-04-1P

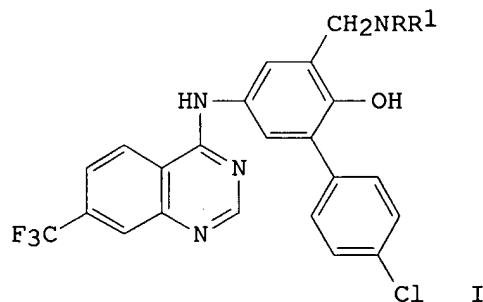
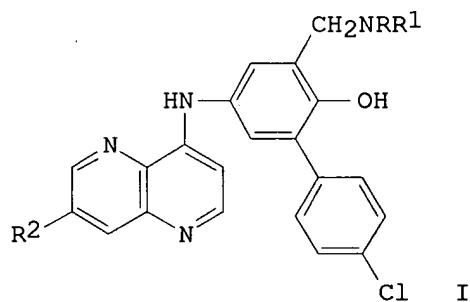
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for bradycardic)

RN 133062-04-1 HCPLUS

CN 2,4-Quinazolinediamine, N4-ethyl-N4-phenyl- (9CI) (CA INDEX NAME)

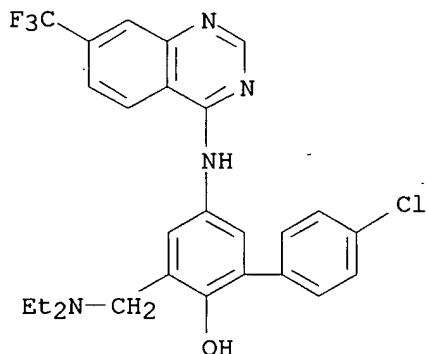


L6 ANSWER 136 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:6439 HCAPLUS
 DOCUMENT NUMBER: 114:6439
 TITLE: Potential antimalarials. XII. 4-Chloro-3-(substituted amino)methyl-5-[7-bromo and 7-trifluoromethyl)-1,5-naphthyridin-4-ylamino]biphenyl-2-ols and 4-chloro-3-(substituted amino)methyl-5-(7-trifluoromethylquinazolin-4-ylamino)biphenyl-2-ols
 AUTHOR(S): Barlin, Gordon B.; Jiravinyu, Chuenjit
 CORPORATE SOURCE: John Curtin Sch. Med. Res., Aust. Natl. Univ.,
 Canberra, 2601, Australia
 SOURCE: Australian Journal of Chemistry (1990), 43(8), 1367-73
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CODEN: AJCHAS; ISSN: 0004-9425
 GI

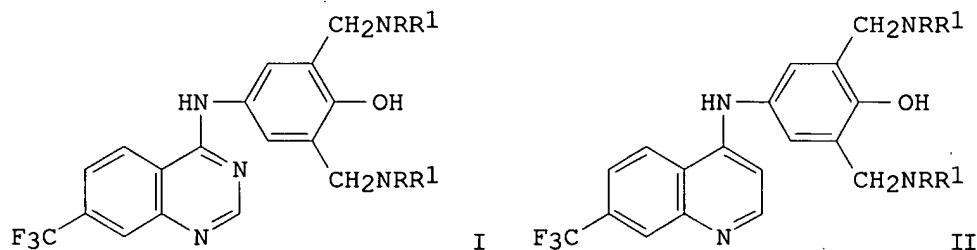


AB The title compds. I and II ($R = H$, $R1 = CMe_3$; $R = R1 = Et$; $NRR1 =$ pyrrolidin-1-yl, piperidin-1-yl, 3-methylpiperidin-1-yl, 4-methylpiperidin-1-yl, 4-benzylpiperidin-1-yl, 4-benzylpiperazin-1-yl; $R2 = Br, F_3C$) were prepared by substitution of the appropriate chloro heterocycle with an aminobiphenyl. The antimalarial activity of I and II

was tested against chloroquine-sensitive isolate of *Plasmodium falciparum*.
 IT 130806-69-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and antimalarial activity of)
 RN 130806-69-8 HCAPLUS
 CN [1,1'-Biphenyl]-2-ol, 4'-chloro-3-[(diethylamino)methyl]-5-[[7-(trifluoromethyl)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 137 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1990:515237 HCAPLUS
 DOCUMENT NUMBER: 113:115237
 TITLE: Potential antimalarials. IX. Di-Mannich bases of 4-(7'-trifluoromethylquinazolin-4'-ylamino)phenol and 4-(7'-trifluoromethylquinolin-4'-ylamino)phenol
 AUTHOR(S): Barlin, Gordon B.; Jiravinyu, Chuenjit
 CORPORATE SOURCE: John Curtin Sch. Med. Res., Aust. Natl. Univ., Canberra, 2601, Australia
 SOURCE: Australian Journal of Chemistry (1990), 43(2), 311-19
 CODEN: AJCHAS; ISSN: 0004-9425
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 113:115237
 GI



AB Title Mannich bases I [NRR1 = NET2, NPr2, NMeBu, N(C6H11)2, pyrrolidin-1-yl, piperidin-1-yl, 3-methylpiperidin-1-yl, 3,5-dimethylpiperidin-1-yl, 4-benzylpiperidin-1-yl] and II [NRR1 = NMeBu, N(C6H11)2] were prepared. When tested for antimalarial activity against *Plasmodium falciparum* in vitro, the quinazolines were rather less active.

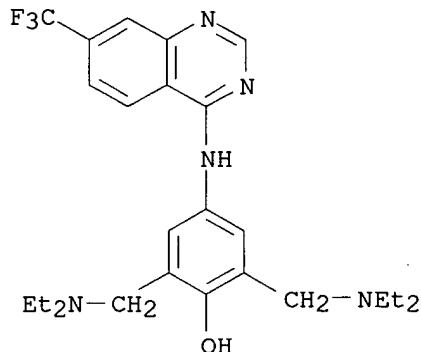
than the corresponding quinolines.

IT 129190-29-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

RN 129190-29-0 HCPLUS

CN Phenol, 2,6-bis[(diethylamino)methyl]-4-[[7-(trifluoromethyl)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 138 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:509005 HCPLUS

DOCUMENT NUMBER: 113:109005

TITLE: Frequency- and voltage-dependent effects of changrolin on maximal upstroke velocity of action potentials in guinea pig papillary muscles

AUTHOR(S): Pan, Hui; Shen, Weiqun; Yu, Zhiming; Xu, Bin

CORPORATE SOURCE: Dep. Physiol., Suzhou Med. Coll., Suzhou, 215007, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1990), 11(4), 317-21

CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Changrolin (CRL) is a new antiarrhythmic drug originated in China in 1970s. The effects of CRL on maximal upstroke velocity (Vmax) of action potentials were studied with standard microelectrode and computer in guinea pig papillary muscles. CRL depressed the Vmax. This effect was dependent on the rate of stimulations. The onset of use-dependent depression was monoexponential and dependent on drug concentration and rate of stimulations. The rate of recovery from use-dependent depression also followed a single exponential time course. CRL shifted the curve relating normalized Vmax to membrane potential in the hyperpolarizing direction. These suggest that CRL belongs to class I antiarrhythmic drugs.

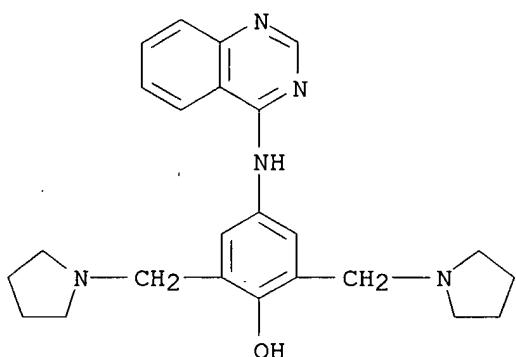
IT 72063-47-9, Changrolin

RL: BIOL (Biological study)

(heart elec. activity response to, antiarrhythmic action in relation to)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 139 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:417689 HCAPLUS

DOCUMENT NUMBER: 113:17689

TITLE: Rate-dependent depression of maximal rate of depolarization in guinea pig papillary muscle action potentials by changrolin

AUTHOR(S): Kuang, Yan; Liu, Tianpei

CORPORATE SOURCE: Dep. Pharmacol., Nanjing Med. Coll., Nanjing, 210005, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1990), 11(3), 225-9
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The rate-dependent block (RDB) of changrolin on the maximal rate of depolarization (V_{max}) of action potentials was studied in guinea pig right ventricular papillary muscles. The result was compared with that of class IA (quinidine), IB (mexiletine) and IC (lorcainide) antiarrhythmics in order to classify changrolin. Mexiletine exhibited the fastest response in the onset rate of RDB. V_{max} Reached 61% of its final value by the second beat during a train of stimuli. In response to a similar train of stimuli, quinidine, lorcainide and changrolin produced exponential falls of V_{max} with the consts. of -0.143, -0.085 and -0.051 AP-1 (AP = action potentials), resp. The time consts. of recovery for mexiletine, quinidine, lorcainide and changrolin were .apprx. 1.58, 9.06, 13.37 and 55.16 s. Apparently the kinetics of RDB with changrolin are similar to those of IC antiarrhythmics.

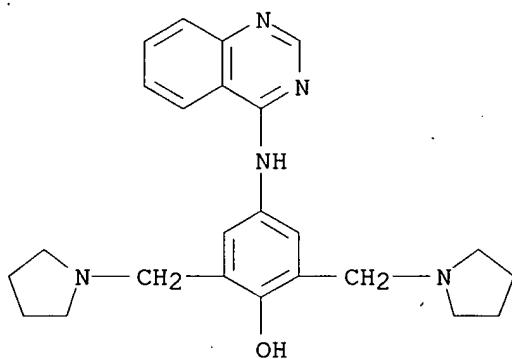
IT 72063-47-9, Changrolin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of, classification of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 140 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:235262 HCPLUS

DOCUMENT NUMBER: 112:235262

TITLE: Synthesis of 1,4-disubstituted piperazines as potential antihypertensive agents

AUTHOR(S): Abou-Zeid, K. A. M.; Youssef, K. M.; Amine, F. M.; Botros, S.; Isaac, Z.

CORPORATE SOURCE: Fac. Pharm., Cairo Univ., Egypt

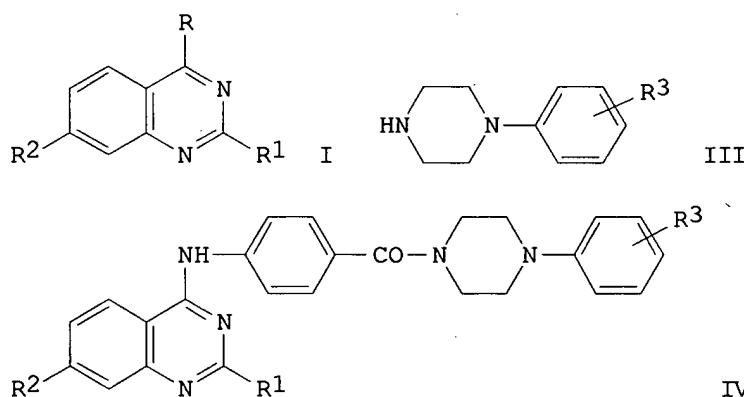
SOURCE: Egyptian Journal of Pharmaceutical Sciences (1989), 30(1-4), 429-36

CODEN: EJPSBZ; ISSN: 0301-5068

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB 4-Chloroquinazolines I (R = Cl; R₁ = H, Me; R₂ = H, Cl) were reacted with 4-H₂NC₆H₄CO₂H to give N-(4-quinazolinyl)aminobenzoic acids (I; R = NHC₆H₄CO₂H-4) (II). II were treated with SOCl₂ and 1-arylpiperazines III (R = 4-Cl, 4-Br, 1-Me, 4-Fl, H) to give benzamides IV. IV did not exhibit hypotensive activity in anesthetized normotensive cats.

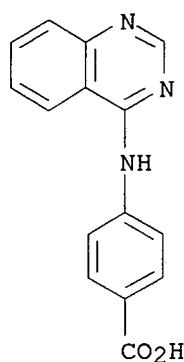
IT 127222-24-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and amidation of, with thionyl chloride and arylpiperazines)

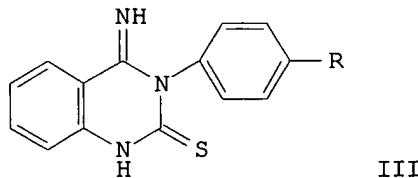
RN 127222-24-6 HCPLUS

CN Benzoic acid, 4-(4-quinazolinylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 141 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1990:118750 HCPLUS
 DOCUMENT NUMBER: 112:118750
 TITLE: A new knowledge about the synthesis of
 1-phenyl-3-(2-cyanophenyl)thiourea
 AUTHOR(S): Pazdera, P.; Novacek, E.; Ondracek, D.
 CORPORATE SOURCE: Fac. Nat. Sci., J. E. Purkyne Univ., Brno, CS-611 37,
 Czech.
 SOURCE: Chemical Papers (1989), 43(3), 465-70
 DOCUMENT TYPE: CODEN: CHPAEG; ISSN: 0366-6352
 LANGUAGE: Journal
 English
 GI



III

AB The addition of 2-H₂NC₆H₄CN (I) to 4-RC₆H₄NCS (II, R = H) by the literature procedure (Taylor, E. C.; Ravindranathan, R. V., 1962) did not lead to 2-NCC₆H₄NHCSN₂Ph, but to its cyclization product tetrahydroquinazolinethione III (R = H). This was the only addition product formed, even under varied conditions. Similarly, under a variety of conditions, I reacted with II (R = NO₂) to give a single product III (R = NO₂). I was prepared by the addition of PhNH₂ to 2-NCC₆H₄NCS (IV) at room temperature in CH₂Cl₂ and petroleum ether. Previously unknown, IV was prepared by

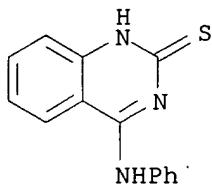
the reaction of Cl₂CS with I in CH₂Cl₂-water.

IT 35696-83-4P

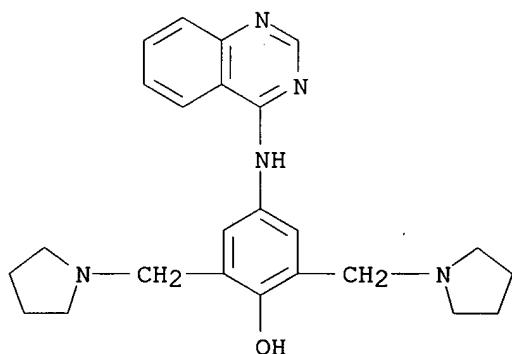
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 35696-83-4 HCPLUS

CN 2(1H)-Quinazolinethione, 4-(phenylamino)- (9CI) (CA INDEX NAME)

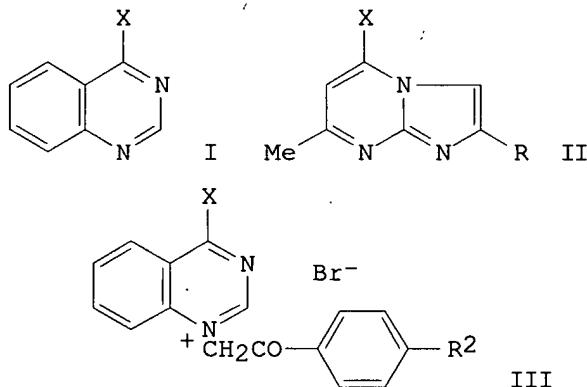


L6 ANSWER 142 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1990:111803 HCAPLUS
 DOCUMENT NUMBER: 112:111803
 TITLE: Electrophysiological effects of changrolin on single ventricular myocytes isolated from adult guinea pig
 AUTHOR(S): Liu, Qiying; Chen, Weizhou; Wei, Pijing; Gu, Peikun; Jin, Zhengjun
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, 200031, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1989), 10(6), 526-9
 DOCUMENT TYPE: CODEN: CYLPDN; ISSN: 0253-9756
 LANGUAGE: Journal Chinese
 AB The effect of changrolin on heart electrophysiolog. was studied in isolated guinea pig single ventricular myocytes. Results indicated that changrolin is a slow-type class I antiarrhythmic.
 IT 72063-47-9
 RL: BIOL (Biological study)
 (arrhythmia inhibition by, heart electrophysiolog. response to)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 143 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1990:98477 HCAPLUS
 DOCUMENT NUMBER: 112:98477
 TITLE: Synthesis, hepatoprotectant activity, and antioxidant activity of N-substituted 4-aminoquinazolines and 5-aminoimidazo[1,2-a]pyrimidines
 AUTHOR(S): Mazur, I. A.; Sinyak, R. S.; Mandrichenko, B. E.; Drogovoz, S. M.; Sarbash, T. F.; Stets, V. R.; Kovalenko, S. I.
 CORPORATE SOURCE: Zaporozh. Med. Inst., Zaporozhe, USSR

SOURCE: Farmatsevtichni Zhurnal (Kiev) (1989), (3), 48-50
 CODEN: FRZKAP; ISSN: 0367-3057
 DOCUMENT TYPE: Journal
 LANGUAGE: Ukrainian
 GI



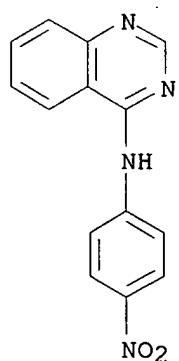
AB Aminating 4-chloroquinazoline (I; X = Cl) and 5-chloro-7-methyl-2-phenyl- and 2-thienylimidazo[1,2-a]pyrimidine (II; X = Cl; R = Ph, thienyl) with R1NH2 [R1 = H, n-C18H37, p-O2NC6H4, H2N, 4-methoxy-9-acridinylamino, o-HOC6H4CONH, isonicotinamido, EtO2CCH2, Et2NCH2CH2, p-Et2NCH2CH2COC6H4, p-[(4,6-dimethyl-2-pyrimidinyl)aminosulfonyl]phenyl, 2,3-dimethyl-1-phenyl-Δ3-pyrrolin-4-yl] in a refluxing polar organic solvent gave 12 corresponding I and II (X = NHR1) in 63-95% yield. I (X = NHC18H37-n, NHC6H4NO2-p) reacted with BrCH2COC6H4R2-p (R2 = H, Br, resp.) to give 52-92% quinazolinium bromides III (same X, R2). II (X = amino) had lower acute toxicity than I (X = amino). Some I and II (X = amino) had hepatotropic and/or antioxidant activity (no data), but most were inactive.

IT 34932-35-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and hepatoprotectant and antioxidant activity of)

RN 34932-35-9 HCPLUS

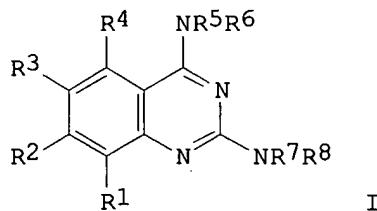
CN 4-Quinazolinamine, N-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 112:21009
 TITLE: Preparation, testing, and formulation of
 2,4-diaminoquinazolines as ulcer inhibitors
 INVENTOR(S): Ife, Robert John; Brown, Thomas Henry; Leach, Colin
 Andrew
 PATENT ASSIGNEE(S): SmithKline Beecham Intercredit BV, Neth.
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 8905297 | A1 | 19890615 | WO 1988-EP1127 | 19881202 |
| W: AU, DK, FI, HU, JP, KR, NO | | | | |
| IL 88507 | A | 19930221 | IL 1988-88507 | 19881127 |
| ZA 8809016 | A | 19891227 | ZA 1988-9016 | 19881201 |
| CN 1033380 | A | 19890614 | CN 1988-108328 | 19881202 |
| EP 322133 | A1 | 19890628 | EP 1988-311461 | 19881202 |
| EP 322133 | B1 | 19910522 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AU 8928230 | A | 19890705 | AU 1989-28230 | 19881202 |
| AU 610328 | B2 | 19910516 | | |
| HU 50322 | A2 | 19900129 | HU 1989-345 | 19881202 |
| HU 203325 | B | 19910729 | | |
| JP 02502462 | T | 19900809 | JP 1989-500330 | 19881202 |
| AT 63742 | T | 19910615 | AT 1988-311461 | 19881202 |
| ES 2032024 | T3 | 19930101 | ES 1988-311461 | 19881202 |
| DK 8903786 | A | 19890802 | DK 1989-3786 | 19890802 |
| NO 8903112 | A | 19891002 | NO 1989-3112 | 19890802 |
| PRIORITY APPLN. INFO.: | | | GB 1987-28336 | A 19871203 |
| | | | GB 1988-20184 | A 19880825 |
| | | | EP 1988-311461 | A 19881202 |
| | | | WO 1988-EP1127 | A 19881202 |

OTHER SOURCE(S): MARPAT 112:21009
 GI



AB The title compds. [I; R1-R4 = H, C1-4 alkyl, alkoxy, alkylthio, alkanoyl, Ph, amino, halo, CF₃; R5-R8 = H, C1-4 alkyl, (substituted) arylalkyl; R5R6N, R7R8N = (unsatd.) ring], useful as gastric acid secretion inhibitors, were prepared Thus, 3-methoxyanthranilic acid (preparation given) in

H₂O/HOAc was treated dropwise with KOCN in H₂O and the mixture was stirred 2 h followed by addition of NaOH and acidification of the resulting salt to give 8-methoxy-2,4-quinazolinedione. The latter was refluxed 5 h with Me₂NC₆H₅ in POCl₃ to give 8-methoxy-2,4-dichloroquinazoline. The latter

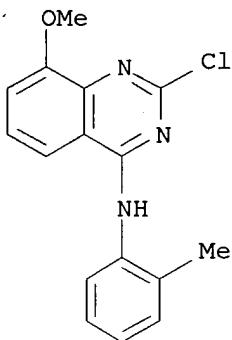
in H₂O/THF was stirred with o-toluidine and NaOAc for 4 d (with addition of NaOH to maintain pH 7) followed by heating of the product with ethanolic NH₃ at 120° to give 2-amino-8-methoxy-4-(2-methylphenylamino)quinazoline. The latter at 10 μmol/kg i.v. in rats gave 60% inhibition of pentagastrin-stimulated gastric acid secretion.

IT 124309-69-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of, by toluidine, in preparation of gastric acid secretion inhibitor)

RN 124309-69-9 HCPLUS

CN 4-Quinazolinamine, 2-chloro-8-methoxy-N-(2-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 145 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:21004 HCPLUS

DOCUMENT NUMBER: 112:21004

TITLE: Preparation, testing, and formulation of
4,5-dihydro-6-aryl-2-oxopyridazines as cardiotonics
and antihypertensives

INVENTOR(S): Nomoto, Yuji; Takai, Haruki; Ohno, Tetsuji; Kubo,
Kazuhiro

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 48 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

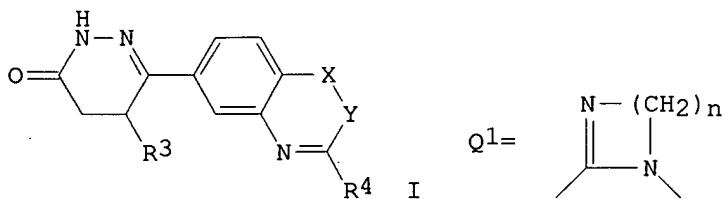
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| EP 326307 | A2 | 19890802 | EP 1989-300611 | 19890123 |
| EP 326307 | A3 | 19900912 | | |
| EP 326307 | B1 | 19940817 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| JP 02022274 | A | 19900125 | JP 1989-7055 | 19890113 |
| US 5063227 | A | 19911105 | US 1990-462914 | 19900111 |
| PRIORITY APPLN. INFO.: | | | JP 1988-13301 | A 19880123 |
| | | | US 1989-297440 | B1 19890117 |

GI



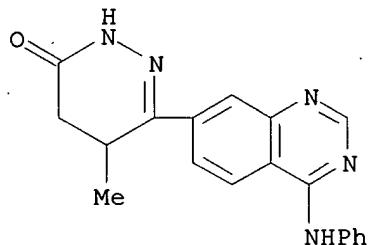
AB The title compds. [I; R₁,R₂ = H, (substituted) alkyl, alkenyl, aralkyl, aryl, amino, alkoxy carbonylamino, pyridylalkyl; NR₁R₂ = heterocyclyl; R₃ = H, alkyl; R₄ = H, SH, OH, (substituted) alkyl, alkylthio, alkoxy, NR₁R₂; R₅ = H, alkyl, NR₁R₂; X - Y = CH₂NH, R₅C:N, Q₁, etc.; n = 2,3], useful as cardiotonics and antihypertensives, were prepared. Thus, 3-(4-bromo-3-nitrobenzoyl)butyric acid (prepn given) was cyclocondensed with N₂H₄ in HOAc to give 100% 6-(4-bromo-3-nitrophenyl)-4,5-dihydro-5-methyl-3(2H)pyridazinone. The latter was cyanated with CuCN in DMF (44%) followed by reduction with SnCl₂/HCl to give 87% 6-(3-amino-4-cyanophenyl)-4,5-dihydro-5-methyl-3(2H)pyridazinone. This was condensed with (EtO)₃CH to give 24% of the 3-ethoxymethyleneamino derivative, which was cyclized in MeOH containing MeNH₂ to give the corresponding pyridazinone, which was heated with 2N NaOH to give 76% 4,5-dihydro-5-methyl-6-(4-methylaminoquinazolin-7-yl)-3(2H)pyridazinone. The latter at 0.03 mg/kg i.v. in dogs increased myocardial contractility with a Δ dp/dt of 78.3%.

IT 124294-54-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cardiotonic and antihypertensive)

RN 124294-54-8 HCPLUS

CN 3(2H)-Pyridazinone, 4,5-dihydro-5-methyl-6-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 146 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:608639 HCPLUS

DOCUMENT NUMBER: 111:208639

TITLE: Reversed-phase ion-pair HPLC determination of
changrolin in plasma

AUTHOR(S): Wang, Yuefen; Li, Jie; Zeng, Yanlin

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci.,
Shanghai, Peop. Rep. China

SOURCE: Zhongguo Yiyao Gongye Zazhi (1989), 20(6), 260-3
CODEN: ZYGZEA; ISSN: 1001-8255

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Changrolin was extracted with cyclohexane-CH₂Cl₂-Et acetate (25:20:7) from human or rabbit plasma, and determined by reversed-phase ion-pair HPLC, using 0.01 M HClO₄-MeOH (45:55, pH 2.3) as the mobile phase and detection at 330

nm; the detection limit was 25 ng, the recovery was >87%, and the coefficient of variation was <4.7%.

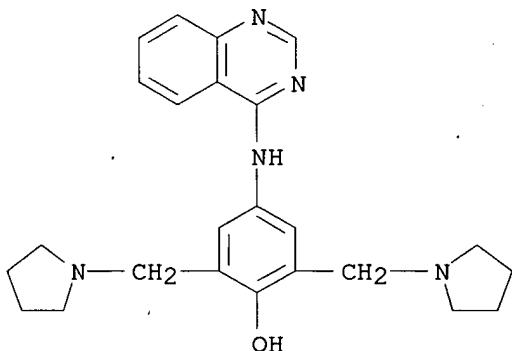
IT 72063-47-9

RL: ANT (Analyte); ANST (Analytical study)

(determination of, in blood plasma of humans and laboratory animals, by HPLC)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 147 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:192855 HCPLUS

DOCUMENT NUMBER: 110:192855

TITLE: Preparation of 4-aminoquinazolines as ulcer inhibitors

INVENTOR(S): Aozuka, Tomoshi; Okubo, Akihiro; Ishii, Katsuyuki; Ishikawa, Mikio; Ueki, Shigeru; Arai, Heihachiro

PATENT ASSIGNEE(S): Zeria Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

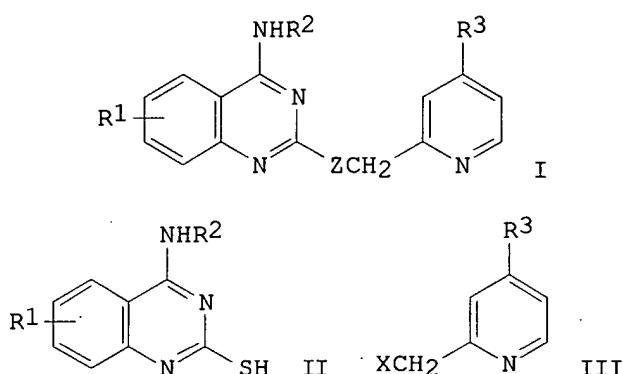
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|------------|-----------------|----------|
| JP 63284172 | A | 19881121 | JP 1987-118398 | 19870515 |
| PRIORITY APPLN. INFO.: | | | JP 1987-118398 | 19870515 |
| OTHER SOURCE(S): | MARPAT | 110:192855 | | |

GI



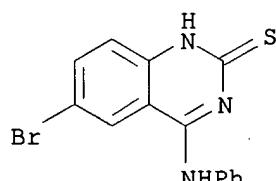
AB Title compds. I [R1 = H, halo, (fluoro)alkyl; R2 = H, alkyl, cycloalkyl, aralkyl, (substituted) Ph; R3 = H, alkyl, (fluoro)alkoxy, PhO, PhCH2O, alkoxy carbonyl, carbamoyl; Z = S, SO] are prepared by, e.g., thioetherification of mercaptoquinazolines II with pyridines III (X = halo, reactive ester residue, i.e. MeSO3, PhSO3, MeC6H4SO3). A mixture of II (R1 = 6-Cl; R2 = Ph) (preparation given), III.HCl (R3 = H; X = Cl), and KOH in EtOH was refluxed to give 66% I (R1 = 6-Cl; R2 = Ph; R3 = H; Z = S), which was oxidized by m-ClC6H4CO2OH in CH2Cl2 to afford 88% I (Z = SO) (IV). IV at 29.0 μ mol/kg p.o. showed 73.3% control of HCl-EtOH-induced ulcer in rats, vs. 8.0% for cimetidine at 119.0 μ mol/kg. Tablets (200 mg) were formulated containing IV 20, lactose 106, corn starch 37, crystalline cellulose 25, Ca CM-cellulose 10, and Mg stearate and sprayed with an enteric coating solution comprising hydroxypropyl Me cellulose phthalate 8.0, myvacet 0.4, CH2Cl2 50.0, and Me2CHOH 41.6 weight%.

IT 102393-98-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and thioetherification of, with pyridylmethyl halide)

RN 102393-98-6 HCPLUS

CN 2(1H)-Quinazolinethione, 6-bromo-4-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 148 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:107868 HCPLUS

DOCUMENT NUMBER: 110:107868

TITLE: Cytotoxic effects of changrolin, lidocaine and amiodarone on the ultrastructure of cultured rat beating cardiac myocytes

AUTHOR(S): Yang, Yingzhen; Yang, Xueyi; Guo, Qi; Jin, Peiying; Chen, Haozhu; Shen, Juying; Peng, Baozhen; Gong, Zuxun; Chen, Weizhou

CORPORATE SOURCE: Shanghai Inst. Cardiovasc. Dis., Shanghai, 200032, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1989), 10(1), 46-8

CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

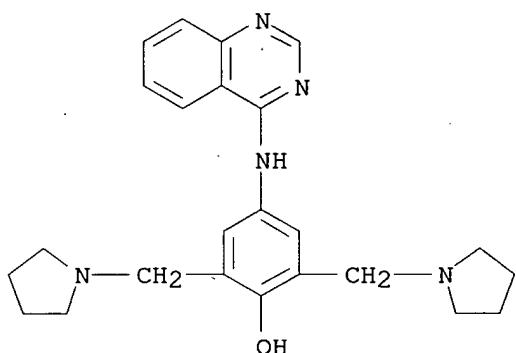
AB Changrolin (25 mg/mL), lidocaine (250 mg/mL), and amiodarone (6.25 mg/mL) at antiarrhythmic concns. caused no or very slight damage to the ultrastructure of cultured rat beating cardiac myocytes; the ultrastructures (mitochondrial membrane, myofibrils, nuclei) of the myocytes were damaged by these drugs at 100, 1000, and 50 mg/mL, resp.

IT 72063-47-9, Changrolin

RL: BIOL (Biological study)
(heart toxicity from, ultrastructure change in)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 149 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:75437 HCPLUS

DOCUMENT NUMBER: 110:75437

TITLE: Synthesis of tritium and carbon-14-labeled changrolin

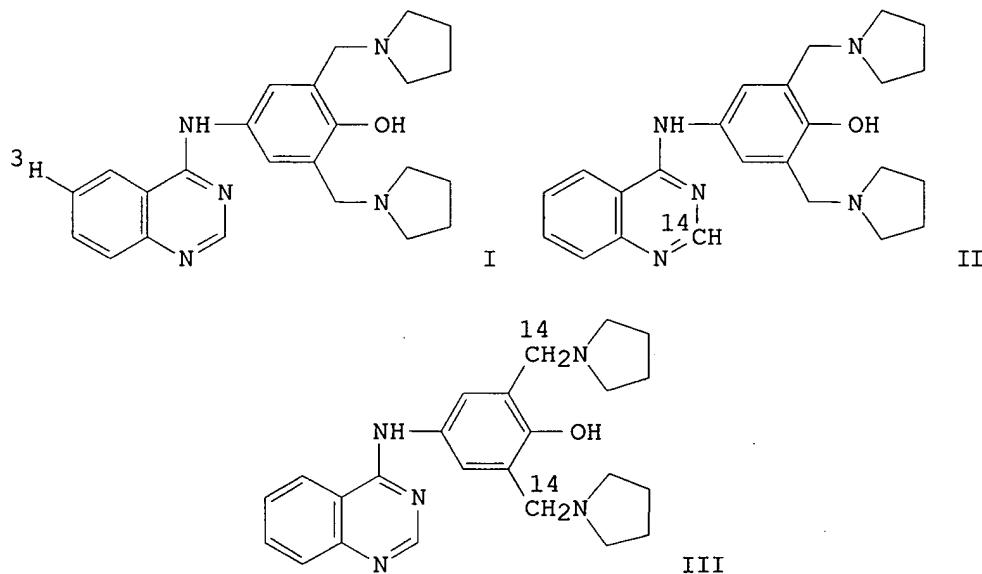
AUTHOR(S): Zhang, Xin; Bao, Yuewen; Ding, Ruiqin

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai,
Peop. Rep. ChinaSOURCE: Hejishu (1988), 11(5), 29-31
CODEN: NUTEDL; ISSN: 0253-3219

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



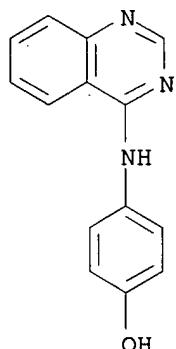
AB Title compds. I, II, and III were prepared E.g., Mannich reaction of 4-(4-hydroxyanilino)quinazoline with $^{14}\text{CH}_2\text{O}$ and pyrrolidine gave III.

IT 34923-98-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(Mannich reaction of, with pyrrolidine)

RN 34923-98-3 HCAPLUS

CN Phenol, 4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 150 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:75427 HCAPLUS

DOCUMENT NUMBER: 110:75427

TITLE: Reaction of 4-quinazolinamines with organolithium
reagents

AUTHOR(S): Johannsen, Frank; Pedersen, Erik B.

CORPORATE SOURCE: Dep. Chem., Odense Univ., Odense, DK-5230, Den.

SOURCE: Chemica Scripta (1987), 27(2), 277-81

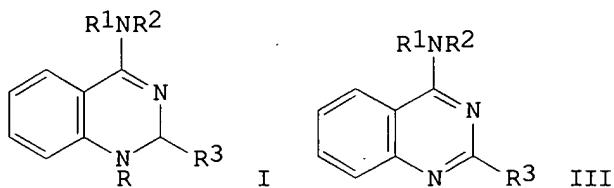
CODEN: CSRPB9; ISSN: 0004-2056

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 110:75427

GI



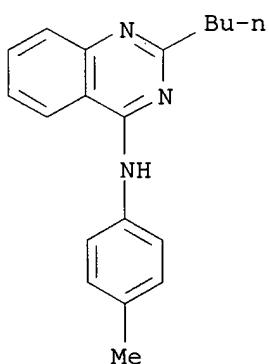
AB 2-Alkyl-1,2-dihydro-4-quinazolinamines I (R = H; R¹ = H, Me; R² = p-tolyl, Me, Ph, CHMe₂, Bu; R³ = Me, Bu, EtCHMe, Me₃C) (II) (16 compds.) were prepared in 43-89% yield by treating 4-quinazolinamines (III, R³ = H) with R³Li in THF. The importance of using an inert atmospheric is demonstrated by expts. where the postulated intermediate (I, R = Li) is exposed to O₂ leading to the aromatized product III. The stability of II towards oxidation and the possibility of using II as a NAD(P)H model is investigated. Insecticide activities were found for II (R¹ = H, R² = p-tolyl, R³ = H) (1 g/m²) against *Anthonomus grandis* adult; for II (R¹ = Me, R² = Ph, R³ = Bu) (12.5 ppm) against *Aedes aegyptii* larvae.

IT 118718-38-0P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and spectra of)

RN 118718-38-0 HCPLUS

CN 4-Quinazolinamine, 2-butyl-N-(4-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 151 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:542277 HCPLUS

DOCUMENT NUMBER: 109:142277

TITLE: Effects of changrolin on arrhythmia in rats

AUTHOR(S): Zhang, Jingxia; Dong, Yueli; Chen, Weizhou

CORPORATE SOURCE: Dep. Pharmacol., Shanghai Second Med. Univ., Shanghai,
Peop. Rep. China

SOURCE: Shanghai Dier Yike Daxue Xuebao (1988), 8(2), 140-2
CODEN: SDDXE3; ISSN: 0258-5898

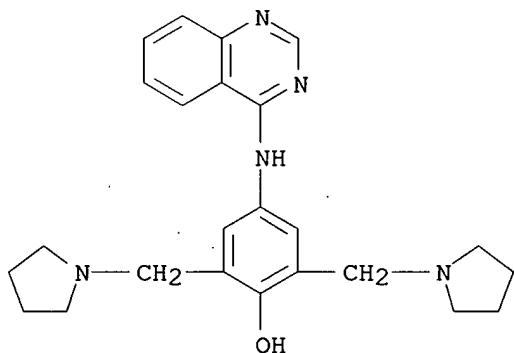
DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Changrolin (i.v. or orally) inhibited ventricular extrasystoles in the early stage in rats following coronary ligation; no ventricular tachycardia and fibrillation were noted. In vitro in noradrenaline-induced ventricular automaticity, the antiarrhythmic effect of changrolin was compared with that of guanidine, propranolol, lidocaine, amiodarone,

and verapamil; the IC₅₀ values were 29.7, 13.2, 0.17, 4.7, 15.5, and 1.8 μM , resp. Apparently, changrolin is useful in the early stage of ventricular arrhythmia in acute myocardial ischemia.

- IT 72063-47-9, Changrolin
 RL: BIOL (Biological study)
 (heart arrhythmia inhibition by)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 152 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:466654 HCAPLUS

DOCUMENT NUMBER: 109:66654

TITLE: Effects of changrolin, pyracrine phosphate, and other drugs on the lipid-facilitated transport of calcium ions in cardiac muscle of rabbit

AUTHOR(S): Chen, Enhong; Yang, Huihua; Pang, Dawei; Zhang, Yuefang; Yao, Renjie

CORPORATE SOURCE: Shanghai Inst. Mater., Chin. Acad. Sci., Shanghai, Peop. Rep. China

SOURCE: Shengwu Huaxue Zazhi (1988), 4(3), 280-6

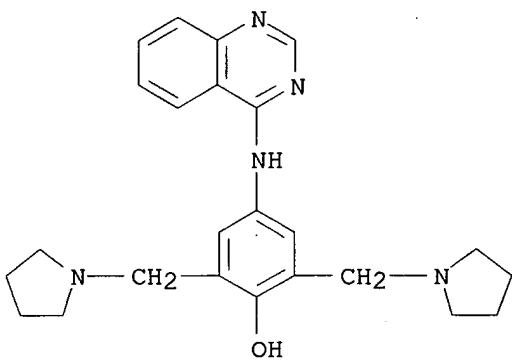
CODEN: SHZAE4; ISSN: 1000-8543

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Changrolin, pyracrine, aconitine, quinidine, hyoscyamine, and verapamil inhibited the lipid-facilitated transport of Ca²⁺ ions in cardiac muscle in a concentration-dependent manner. At 30 $\mu\text{g}/\text{mL}$, the first four drugs showed over 70% inhibition whereas verapamil inhibited Ca²⁺ transport by only 37.8%. Hyoscyamine was only slightly inhibitory.

- IT 72063-47-9, Changrolin
 RL: BIOL (Biological study)
 (lipid-facilitated transport of calcium by heart inhibition by)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 153 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:611496 HCPLUS

DOCUMENT NUMBER: 107:211496

TITLE: Effects of 13 compounds on the activity of globinase and amounts of free amino-acids in Plasmodium berghei

AUTHOR(S): Gu, Haoming; Zhu, Meiyiing; Xi, Guoliang; Chen, Runlian
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci.,
Shanghai, Peop. Rep. ChinaSOURCE: Zhongguo Yaoli Xuebao (1987), 8(5), 460-4
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

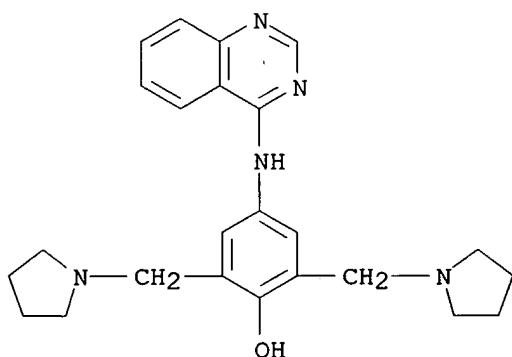
AB The effects of 9 antimalarials and 4 antitumor agents on globinase and the effect of dihydroartemisinin on free amino acids in P. berghei, isolated from the erythrocytes of infected mice, were studied by using [³H]globin as substrate. Artesunate, pyracrini, chloroquine, and changrolin inhibited the proteolysis at 1, 1, 10, and 10 mM, resp., but not at lower concns. 10-Hydroxycomptothecin and FeCl₃ had strong inhibitory effect on the proteolysis. Dihydroartemisinin at 33 mM did not affect the amount of free amino acids.

IT 72063-47-9, Changrolin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(globinase of Plasmodium berghei response to)

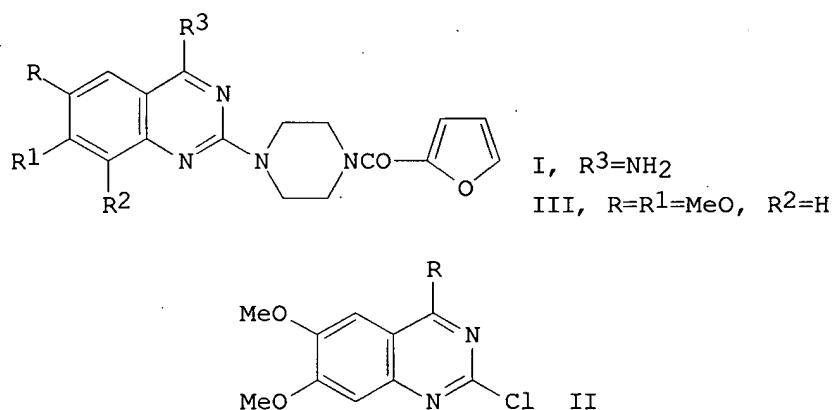
RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 154 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:611447 HCPLUS
 DOCUMENT NUMBER: 107:211447
 TITLE: Synthesis and pharmacological study of prazosin analogs
 AUTHOR(S): Volzhina, O. N.; Azimov, V. A.; Medvedev, B. A.; Kazakov, A. A.; Zhikhareva, G. P.; Bondarenko, V. A.; Yuzhakov, S. D.; Dolgun, O. V.; Mashkovskii, M. D.; Yakhontov, L. N.
 CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst., Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1987), 21(7), 802-7
 DOCUMENT TYPE: CODEN: KHFZAN; ISSN: 0023-1134
 LANGUAGE: Russian
 OTHER SOURCE(S): CASREACT 107:211447
 GI



AB I ($R = 4$, Br, or NO₂; $R^1 = H$ or Cl; $R^2 = H$, Br, or NO₂) were prepared by the reaction of appropriately substituted aminobenzoic acids with urea followed by the conversion of the quinazoline-2,4-diones to 2,4-dichloroquinazolines, amine substitution and reaction with N-furylpiperazine. II [$R = OCH_2CH(OH)CH_2NHCHMe_2$ or NHC₆H₄[OCH₂CH(OH)NHCHMe₂]-3(or 4) were prepared by the reaction of 2,4-dichloro-6,7-dimethoxyquinazoline with 2-phenyl-3-isopropyl-5-hydroxymethyloxazolidine or 3 (or 4)-(3-isopropylamino-2-hydroxypropoxy)aniline. Further reaction of II with N-furylpiperazine gave III (R^3 is same as R for II). In anesthetized cats, I ($R = R^2 = H$, $R^1 = Cl$), III [$R^3 = OCH_2CH(OH)CH_2NHCHMe_2$ and $R^3 = NHC_6H_4[OCH_2CH(OH)NHCHMe_2]-3$ (or 4)] at 0.5 or 5' mg/kg decreased the arterial blood pressure by 10-40% based on starting conditions. The duration of the action was ≤ 30 min. In anesthetized rats, the same compds. at comparatively higher doses caused hypotensive activity. These compds. showed α -adrenergic blocking activity in anesthetized cats and the duration was ≤ 30 min. Structure-activity relations are discussed.

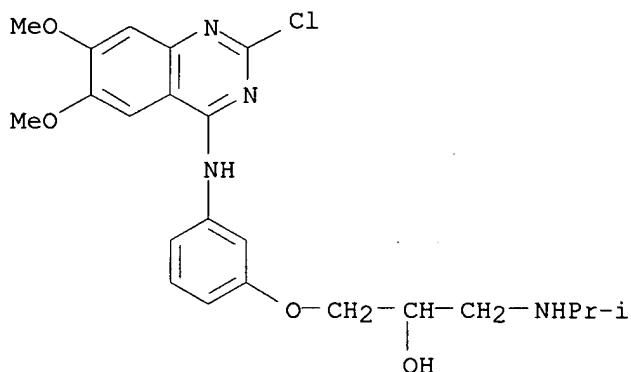
IT 111218-77-0P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (preparation and pharmacol. of)

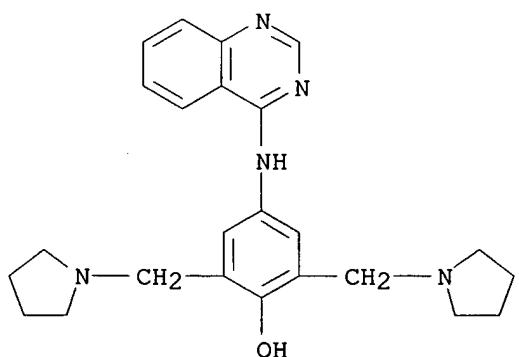
RN 111218-77-0 HCPLUS

CN 2-Propanol, 1-[3-[(2-chloro-6,7-dimethoxy-4-quinazolinyl)amino]phenoxy]-3-

[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

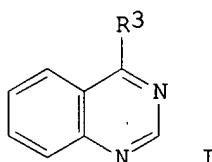


L6 ANSWER 155 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:611361 HCPLUS
 DOCUMENT NUMBER: 107:211361
 TITLE: Determination of changrolin by quantitative TLC scanning technique
 AUTHOR(S): Wang, Yuefen; Shu, Hanlin; Zeng, Yanlin
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. China
 SOURCE: Yaowu Fenxi Zaishi (1987), 7(4), 221-3
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB Changrolin in rabbit plasma was extracted with petroleum ether-CH₂Cl₂ (2:1) and determined by thin-layer chromatog., using Et acetate-EtOH-NH₄OH (25:2.5:2.4) as developing agent and scanning at 254 nm. The recovery and coefficient of variation were 108.4 and 6.4%, resp.
 IT 72063-47-9
 RL: ANT (Analyte); ANST (Analytical study)
 (determination of, in blood plasma by thin-layer chromatog. scanning)
 RN 72063-47-9 HCPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

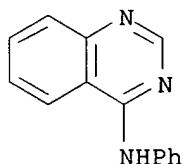


L6 ANSWER 156 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:598230 HCPLUS
 DOCUMENT NUMBER: 107:198230

TITLE: Phosphorus pentoxide in organic synthesis 25. New one-step synthesis of 4-aminoquinazolines. Comparison between mass spectra of 4-aminoquinazolines and 6-aminopurines
 AUTHOR(S): Grgis, Nabih S.; Moeller, Joergen; Pedersen, Erik B.
 CORPORATE SOURCE: Dep. Chem., Odense Univ., Odense, DK-5230, Den.
 SOURCE: Chemica Scripta (1986), 26(4), 617-21
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 107:198230
 GI

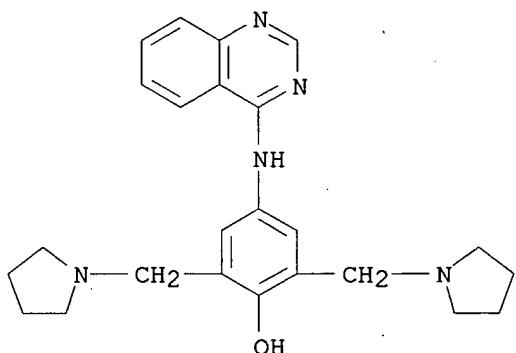


AB Amination of 4(3H)-quinazolinone with $\text{RC}_6\text{H}_4\text{NH}_2 \cdot \text{HCl}$ ($\text{R} = \text{H}, 2\text{-Cl}, 3\text{-, 4-Me}, 2,6\text{-Me}_2$) or $\text{R}_1\text{R}_2\text{NH}$ ($\text{R}_1 = \text{H}, \text{R}_2 = \text{n-hexyl, cyclohexyl, PhCH}_2, \text{furfuryl}; \text{R}_1 = \text{R}_2 = \text{n-hexyl}; \text{R}_1 = \text{Me}, \text{R}_2 = \text{Ph}; \text{R}_1\text{R}_2\text{N} = \text{piperidino, morpholino}$) in $\text{N,N-dimethylcyclhexylamine}$ with P_2O_5 , gave 30-89% aminoquinazolines I ($\text{R}_3 = \text{NHC}_6\text{H}_4\text{R}, \text{NR}_1\text{R}_2$).
 IT 34923-95-0P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (preparation and spectra of)
 RN 34923-95-0 HCPLUS
 CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)

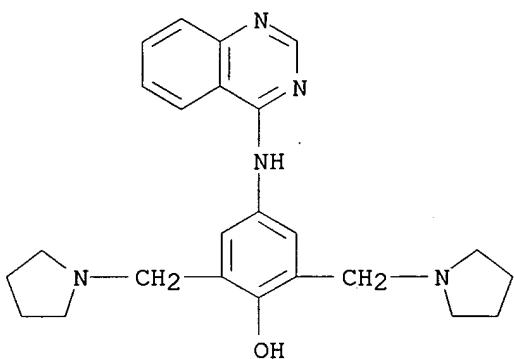


L6 ANSWER 157 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:568530 HCPLUS
 DOCUMENT NUMBER: 107:168530
 TITLE: Electrophysiologic effects of changrolin on heart conduction in anesthetized rabbits
 AUTHOR(S): Yu, Ying; Yu, Fangshu; Gu, Peikun; Jin, Zhenjun
 CORPORATE SOURCE: Dep. Pharmacol., Shanghai 2nd Med. Univ., Shanghai,
 Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1987), 8(5), 421-5
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB The electrophysiologic effects of changrolin on the heart conductive system were compared with those of procainamide in anesthetized rabbits. Changrolin decreases ventricular excitability throughout the cardiac cycle, whereas procainamide decreases the excitability in the early diastole. The antiarrhythmic effect of changrolin is discussed.

IT 72063-47-9, Changrolin
 RL: BIOL (Biological study)
 (heart conduction response to, antiarrhythmic effect in relation to)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 158 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:547028 HCAPLUS
 DOCUMENT NUMBER: 107:147028
 TITLE: Pharmacodynamic and pharmacokinetic study on the antiarrhythmic effect of a combination of propranolol and changrolin
 AUTHOR(S): Zhang, Caili; Pan, Xingyuan; Zhao, Ming; Zhang, Jingyan; Chen, Kangmei
 CORPORATE SOURCE: Dep. Pharmacol., Tianjin Med. Coll., Tianjin, Peop. Rep. China
 SOURCE: Tianjin Yiyao (1987), 15(5), 259-63
 CODEN: TIYADG; ISSN: 0253-9896
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB The effects of changrolin, propranolol and combination of these drugs on the aconitine-induced arrhythmia in rats were studied. Antiventricular premature systole response was additive with the combined treatments. Anti-ventricular fibrillation response was synergistic with the combined treatment. Plasma levels of propranolol were not different between single and combination therapy groups.
 IT 72063-47-9, Changrolin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (antiarrhythmic activity of propranolol combination with)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 159 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:534278 HCAPLUS

DOCUMENT NUMBER: 107:134278

TITLE: Studies on drugs for coronary diseases. III.
Synthesis of some Mannich bases of substituted
aminophenols

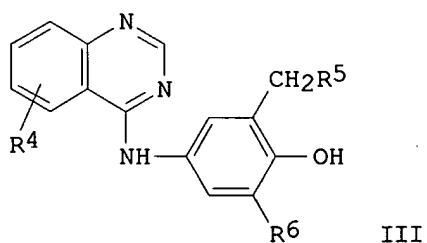
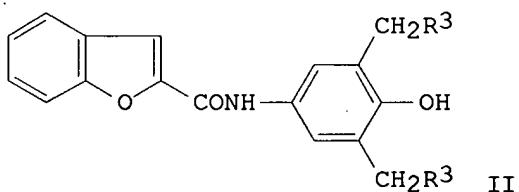
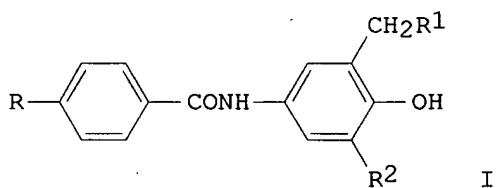
AUTHOR(S): Kang, Aili; Sun, Cunji

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai,
Peop. Rep. ChinaSOURCE: Yaoxue Xuebao (1986), 21(12), 892-8
CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI

AB Changrolin analogs I (R = 4-MeO, 4-NO₂, 4-Me, 4-Cl, 4,5-CH₂O₂; R₁ = Me₂N, Et₂N, pyrrolidino, piperidino, morpholino; R₁ = H, CH₂R₁), II (R₃ = NMe₂,

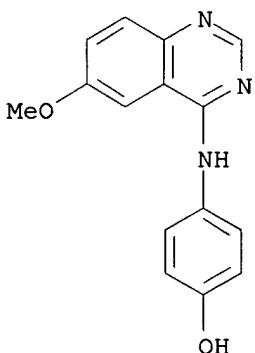
pyrrolidino, piperidino, morpholino), and III ($R_4 = 6,7\text{-CH}_2\text{O}_2$, $R_5 = \text{NMe}_2$, NEt_2 , pyrrolidino, piperidino, morpholino; $R_6 = \text{H}$, CH_2R_1) were prepared I ($R = \text{MeO}$, $R_1 = \text{pyrrolidino}$, $R_2 = \text{CH}_2\text{R}_1$) showed protective effect against aconitine-induced arrhythmia.

IT 110361-10-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Mannich reaction of)

RN 110361-10-9 HCPLUS

CN Phenol, 4-[(6-methoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 160 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:458979 HCPLUS

DOCUMENT NUMBER: 107:58979

TITLE: X-ray crystallographic study on a new drug Changrolin

AUTHOR(S): Wang, Peiling; Li, Deyu; Wu, Jian

CORPORATE SOURCE: Shanghai Inst. Ceram., Acad. Sin., Shanghai, Peop. Rep. China

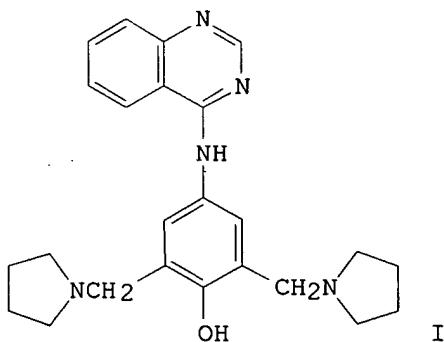
SOURCE: Yingyong Kexue Xuebao (1986), 4(4), 370-2

CODEN: YKXUD4; ISSN: 0255-8297

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



I

AB The crystal structure of antiarrhythmic Changrolin (I) was determined

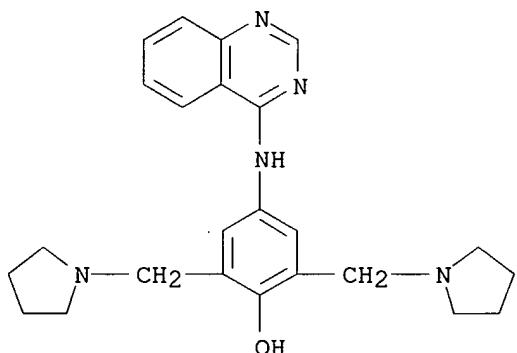
IT 72063-47-9, Changrolin

RL: PRP (Properties)

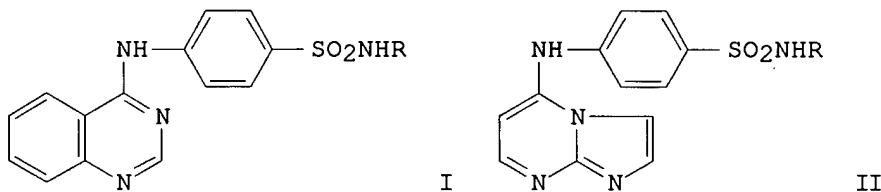
(crystal structure of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 161 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:196388 HCAPLUS
 DOCUMENT NUMBER: 106:196388
 TITLE: Synthesis and biological activity of N-(4-quinazolyl- and 5-imidazopyrimidinyl-) sulfanilamides
 AUTHOR(S): Mazur, I. A.; Sinyak, R. S.; Mandrichenko, B. Yu.; Stoyanovich, S. S.; Stets, V. R.; Steblyuk, P. N.; Kovalenko, S. I.
 CORPORATE SOURCE: Zaporozh. Med. Inst., Zaporozhe, USSR
 SOURCE: Farmatsevtichniy Zhurnal (Kiev) (1987), (1), 58-60
 DOCUMENT TYPE: CODEN: FRZKAP; ISSN: 0367-3057
 LANGUAGE: Journal
 Ukrainian
 GI

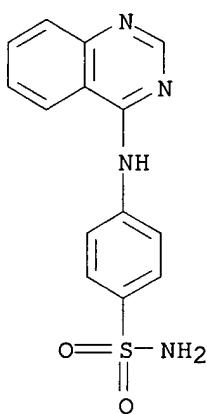


AB Eight quinazolyl- (I) and 5 imidazopyrimidylsulfanilamides (II) ($R = H$, acyl, heterocyclic group, etc.) were synthesized by reaction of 4-chloroquinazoline and 5-chloro-2-phenyl-7-methylimidazopyrimidine, resp., with various sulfanilamides. The yield of the synthesis is 66-99%. The toxicity in mice of compds. obtained was 150-335 mg/kg i.p. The compds. showed anti-inflammatory and analgesic effects, and in concns. 125-500 μ g/mL also antimicrobial action.

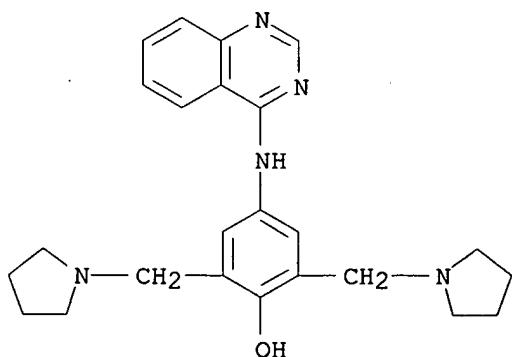
IT 108203-47-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and pharmacol. of)

RN 108203-47-0 HCAPLUS

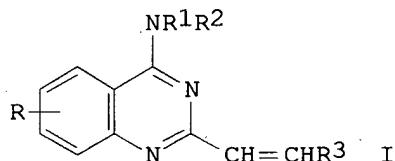
CN Benzenesulfonamide, 4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 162 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:149212 HCPLUS
 DOCUMENT NUMBER: 106:149212
 TITLE: Cytotoxic effects of changrolin, lidocaine and amiodarone on cultured rat beating heart cells
 AUTHOR(S): Yang, Yingzhen; Yang, Xueyi; Guo, Qi; Jin, Peiying; Chen, Juanru; Chen, Weizhou
 CORPORATE SOURCE: Shanghai Inst. Cardiovasc. Dis., Shanghai Med. Univ., Shanghai, 200032, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1987), 8(2), 135-8
 CODEN: CYLPDN; ISSN: 0253-9756
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB Changrolin [72063-47-9] at $\leq 25 \mu\text{g/mL}$ (equivalent to dosages used for antiarrhythmia) caused no cytotoxic effects including morphol. changes and aspartate aminotransferase (AST) [9000-97-9] release in cultured rat beating heart cells. Cytotoxic effects were noted with changrolin at $50 \mu\text{g/mL}$, and at $100 \mu\text{g/mL}$, the beating myocytes were stopped, the configuration and fine structures of the myocytes were destroyed, and AST release was increased; the cytotoxic effect of changrolin was 10 times higher and 4 times lower than that of lidocaine [137-58-6] and amiodarone [1951-25-3], resp.
 IT 72063-47-9, Changrolin
 RL: BIOL (Biological study)
 (heart cytotoxicity from)
 RN 72063-47-9 HCPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

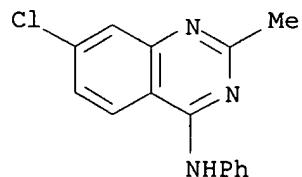


L6 ANSWER 163 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1987:32975 HCAPLUS
 DOCUMENT NUMBER: 106:32975
 TITLE: 4-Amino-2-styrylquinazolines - a new class of
 antiprotozoal drugs
 AUTHOR(S): Moskalenko, N. Yu.; Yakhontov, L. N.; Zhikhareva, G.
 P.; Pershin, G. N.; Peters, V. V.; Evstratova, M. I.;
 Mastafanova, L. I.; Rabinovich, S. A.; Maksakovskaya,
 E. V.; Kulikovskaya, I. M.
 CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst. im.
 Ordzhonikidze, Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1986), 20(4),
 437-46
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 OTHER SOURCE(S): CASREACT 106:32975
 GI



AB 4-Amino-2-styrylquinazolines (I, R = H, 6-OMe, 7-Cl or 6-NO₂; NR₁R₂ = NHCHMe(CH₂)₃NET₂, Et₂N, piperidino or PhNH; and R₃ = 4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 2-anisyl, 2-(2-nitrofuryl), or halophenyl, etc.,) were prepared by the reaction of the corresponding N-substituted-2-methylquinazolines with suitable aldehydes. Various pharmacol. activities of these compds., e.g., trypanosomicidal, amebicidal, protozoacidal, antimalarial, etc., were determined. The LD₅₀ for these compds. are tabulated. Against protozoal infections, 4-(8-diethylamino- α -methylbutylamino)-2-styrylquinazoline with a p-nitro group in the styrene ring showed the highest activity. Replacement of the nitro group by halogen atoms decreased the protozoacidal activity. The presence of the 4-8-diethylamino- α -methylbutylamino group in styrylquinazolines is necessary for exhibiting the antileishmaniasis activity. Other structure-activity correlations are discussed.

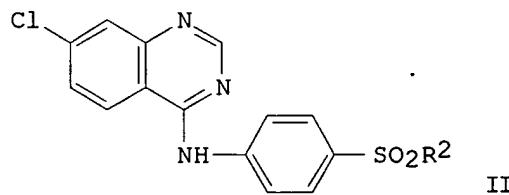
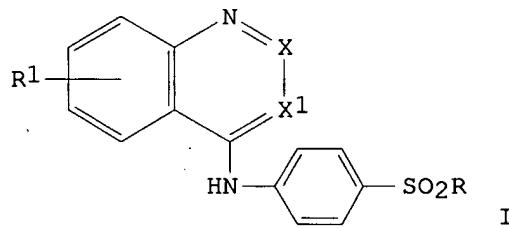
IT 57942-23-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (condensation of, with aldehydes)
 RN 57942-23-1 HCPLUS
 CN 4-Quinazolinamine, 7-chloro-2-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 164 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1986:608903 HCPLUS
 DOCUMENT NUMBER: 105:208903
 TITLE: Quinazoline and cinnoline derivatives
 INVENTOR(S): Boyle, John Terence Arnott; Todd, Richard Simon
 PATENT ASSIGNEE(S): John Wyeth and Brother Ltd., UK
 SOURCE: Brit. UK Pat. Appl., 13 pp.
 CODEN: BAXXDU
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------------|-----------------|----------|
| GB 2160201 | A | 19851218 | GB 1985-14648 | 19850610 |
| GB 2160201 | B | 19880511 | | |
| US 4640920 | A | 19870203 | US 1985-744364 | 19850613 |
| GB 2168977 | A | 19860702 | GB 1985-30586 | 19851212 |
| GB 2168977 | B | 19871021 | | |
| US 4695574 | A | 19870922 | US 1985-809996 | 19851217 |
| US 4734510 | A | 19880329 | US 1986-916984 | 19861009 |
| GB 2191489 | A | 19871216 | GB 1987-16248 | 19870710 |
| GB 2191489 | B | 19880511 | | |
| US 4808715 | A | 19890228 | US 1988-141178 | 19880106 |
| PRIORITY APPLN. INFO.: | | GB 1984-15174 | A | 19840614 |
| | | GB 1984-32091 | A | 19841219 |
| | | GB 1985-14648 | A3 | 19850610 |
| | | US 1985-744364 | A3 | 19850613 |
| | | US 1986-916984 | A3 | 19861009 |

OTHER SOURCE(S): CASREACT 105:208903; MARPAT 105:208903
 GI



AB The title compds. (I; R = amino, substituted N-heterocyclyl; R1 = H, F3C; 1 of X, X1 = N, the other = CH) were prepared as antihypertensives. Thus, 4-H2NC6H4SO3H·H2O was condensed with 4,7-dichloroquinazoline to give (quinazolinylamino)benzenesulfonate II (R2 = OH). This was converted to the acid chloride and treated with H2NCH2CH2NET2 to give II (R =

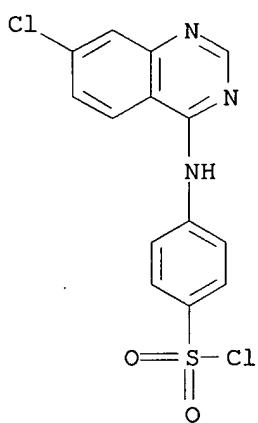
NHCH₂CH₂NET₂) (III). In rats 0.03 mmol III/kg orally decreased blood pressure 33% after 6 h.

IT 105037-37-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)

RN 105037-37-4 HCPLUS

CN Benzenesulfonyl chloride, 4-[(7-chloro-4-quinazolinyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 165 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1986:224869 HCPLUS

DOCUMENT NUMBER: 104:224869

TITLE: Some reactions of nitrogen nucleophiles with
6-bromo-2,4-dichloroquinazoline, 6-bromo-2-chloro-3-methyl-4(3H)-quinazolinone, and 6-bromo-4-chloro- or
(6-bromo-4-chloro-1-phenyl)-1H-quinazoline-2-thione

AUTHOR(S): Sayed, M. A.; El-Gendy, A. M.; El-Fargy, A. F.

CORPORATE SOURCE: Fac. Sci., Ain Shams Univ., Egypt

SOURCE: Pakistan Journal of Scientific and Industrial Research
(1985), 28(6), 367-71

CODEN: PSIRAA; ISSN: 0030-9885

DOCUMENT TYPE: Journal

LANGUAGE: English

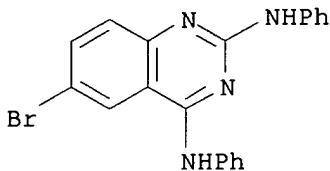
AB Reaction of the title chloroquinazolines with amines and NH₂NH₂ gave the corresponding amino derivs.

IT 102393-88-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

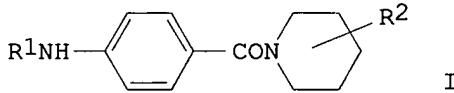
RN 102393-88-4 HCPLUS

CN 2,4-Quinazolinediamine, 6-bromo-N,N'-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 166 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1986:207174 HCAPLUS
 DOCUMENT NUMBER: 104:207174
 TITLE: Piperidines
 PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|------------------------------|------------------------|
| JP 60226877 | A | 19851112 | JP 1985-4376
GB 1984-1092 | 19850114
A 19840116 |
| PRIORITY APPLN. INFO.: | | | CASREACT 104:207174 | |
| OTHER SOURCE(S): | | | | |
| GI | | | | |

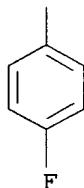
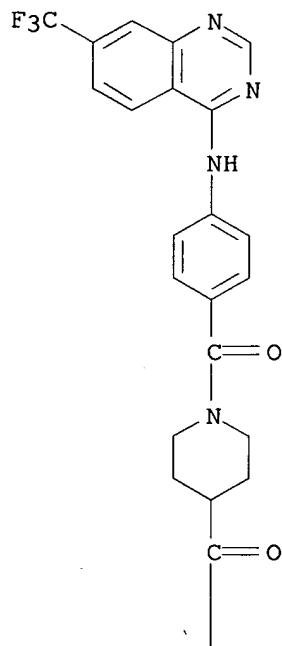


AB The title compds. [I: R1 = (substituted) quinolyl, R2 = (halo)aroyl] and their salts, useful as antihypertensives, were prepared. Thus, stirring a mixture of 0.75 g 4-[[7-(trifluoromethyl)-4-quinolyl]amino]benzoyl chloride-HCl, 0.40 g 4-(4-fluorobenzoyl)piperidine, 0.59 g Et₃N, 23 mL THF, and 11.5 mL CH₂Cl₂ at room temperature for 2 h gave 0.70 g I [R1 = 7-(trifluoromethyl)-4-quinolyl, R2 = 4-(4-fluorobenzoyl)]. I at 10 mg/kg decreased blood pressure in rats by 34-44%.

IT 101931-12-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as antihypertensives)

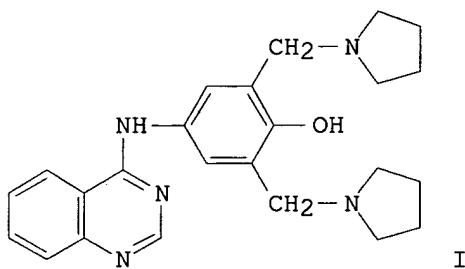
RN 101931-12-8 HCAPLUS

CN Piperidine, 4-(4-fluorobenzoyl)-1-[4-[[7-(trifluoromethyl)-4-quinazolinyl]amino]benzoyl]-, hydrochloride (9CI) (CA INDEX NAME)



• x HCl

L6 ANSWER 167 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:122510 HCPLUS
DOCUMENT NUMBER: 104:122510
TITLE: Autoradiographic studies of the distribution of [14C]changrolin in mice
AUTHOR(S): Chen, Weizhou; Dong, Yueli; Ding, Ruiqin; Zhang, Xin
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (1986), 7(1), 54-5
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



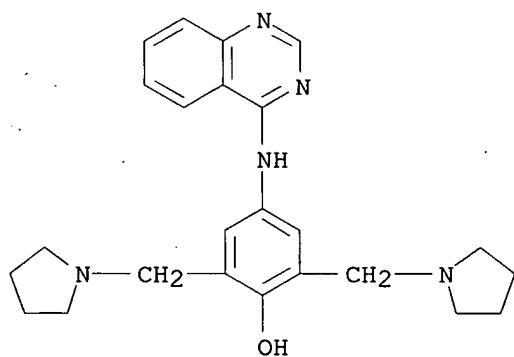
AB 14C-labeled changrolin (I) [72063-47-9] (82 mg/kg) was injected i.v. into mice. At 20 min., radioactivity was highest in the gut and its contents, liver, salivary gland, and lungs, moderate in the kidneys, spleen, and vertebra, and least in the heart, thymus, thyroid, and adrenals. The radioactivity tended to decrease after 2 h, except in the salivary gland and gut, in which an accumulation persisted. After 24 h, no radioactivity was detectable. After i.v. injection of 82 mg/kg/day for 3 days, only a trace of radioactivity was detected in the liver and intestine. Apparently, there was no accumulation within 3 days.

IT 72063-47-9

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 168 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:615311 HCAPLUS

DOCUMENT NUMBER: 103:215311

TITLE: Quinazolines with herbicidal properties

INVENTOR(S): Serban, Alexander; Jensen, Wendy Arne

PATENT ASSIGNEE(S): ICI Australia Ltd., Australia

SOURCE: Pat. Specif. (Aust.), 55 pp.

CODEN: ALXXAP

DOCUMENT TYPE: Patent

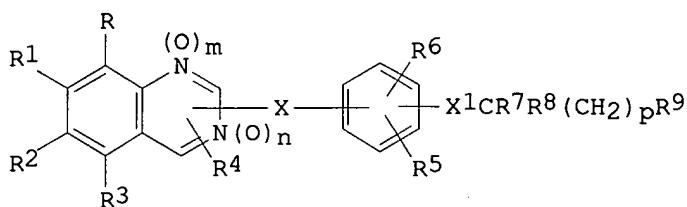
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

| | | | | |
|------------------------|----|---------------------|----------------|----------|
| AU 543008 | B2 | 19850328 | AU 1981-71665 | 19800701 |
| AU 8171665 | A | 19820107 | | |
| US 4675047 | A | 19870623 | US 1981-274165 | 19810616 |
| ZA 8104225 | A | 19820929 | ZA 1981-4225 | 19810622 |
| CA 1140128 | A1 | 19830125 | CA 1981-380648 | 19810626 |
| JP 57046969 | A | 19820317 | JP 1981-103142 | 19810701 |
| JP 05007385 | B | 19930128 | | |
| JP 05039273 | A | 19930219 | JP 1991-250096 | 19910626 |
| JP 06104662 | B | 19941221 | | |
| PRIORITY APPLN. INFO.: | | | AU 1980-4318 | 19800701 |
| OTHER SOURCE(S): | | CASREACT 103:215311 | | |
| GI | | | | |



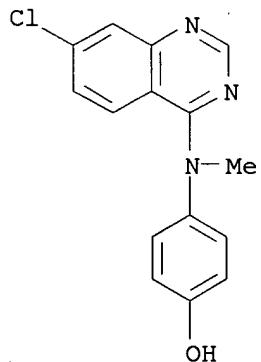
AB The title compds. [I, R-R6 = H, (substituted) alkyl, (substituted) amino, Ph, alkoxy; R7 = H, (substituted) alkyl, alkenyl, acyl; R8 = H, (substituted) alkyl, or R7R8 = alkylidene; R9 = acyl, alkoxy carbonyl; X = O, S, (substituted) imino; X1 = O, S; m, n = 0, 1; p = 0, 1, 2], useful as herbicides (effective at 0.005-20 kg/ha), were prepared. Thus, refluxing a mixture of 1.0 g 2,6-dichloroquinazoline, 0.98 g p-HOC₆H₄OCHMeCO₂Me, 0.76 g K₂CO₃, and 50 mL MeCOEt for 24 h gave Me 2-[4-[(6-chloro-2-quinazolinyl)oxy]phenoxy]propionate.

IT 81585-61-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution reaction of, with bromopropionate)

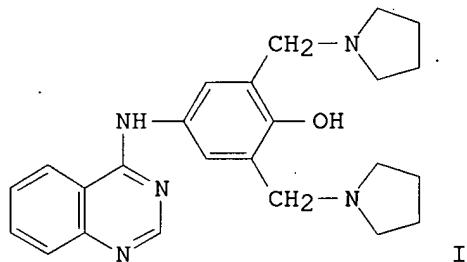
RN 81585-61-7 HCPLUS

CN Phenol, 4-[(7-chloro-4-quinazolinyl)methylamino]- (9CI) (CA INDEX NAME)



L6 ANSWER 169 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:605448 HCPLUS
DOCUMENT NUMBER: 103:205448
TITLE: Clinical pharmacokinetics of antiarrhythmic agent changrolin

AUTHOR(S): Chen, Weizhou; Wang, Changgen; Yang, Xueyi; Cai, Naisheng; Zhu, Junren
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chinese Acad. Sci.,
 Shanghai, Peop. Rep. China
 SOURCE: Yaoxue Xuebao (1985), 20(7), 505-508
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



AB Changrolin (I) [72063-47-9] is a new antiarrhythmic agent. An i.v. drip of changrolin (55 µg/kg/min) for 60 min was given to 11 patients with arrhythmia. The peak concentration was 3.6 µg/mL plasma at the end of the i.v. drips. Except in 3 patients with nodal premature beats, the premature ventricular beats (PVBs) were completely suppressed in 8 patients at 26 min after start of the medication, and the effective plasma concentration of changrolin was 2.6 µg/mL. However, the PVBs reappeared when changrolin level lowered to 2.0 µg/mL in plasma. The pharmacokinetic characteristics of changrolin were found to fit a one-compartment open model. The pharmacokinetic parameters were: elimination rate constant K = 0.032 min⁻¹; t_{1/2} = 24 min; the volume of distribution (Vd) = 0.43 L/kg. The blood pressure and ECG were not changed at a range of 2.7-3.2 µg/mL of changrolin concentration in plasma after an initial bolus of changrolin 50

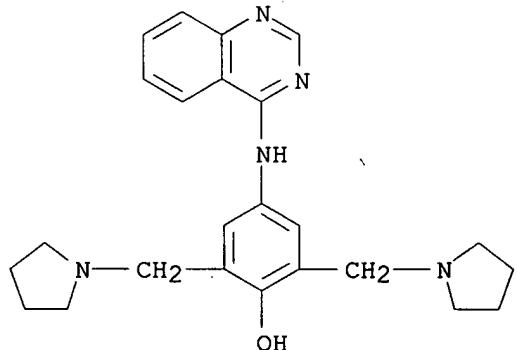
mg was injected into 6 healthy volunteers, followed by an i.v. drip of 40 µg/kg/min for 55 min.

IT 72063-47-9

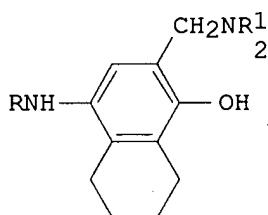
RL: PROC (Process)
 (antiarrhythmic activity and pharmacokinetics of, in humans)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 170 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1985:487753 HCPLUS
 DOCUMENT NUMBER: 103:87753
 TITLE: Synthesis and antimalarial activity of
 2-dialkylaminomethyl-4-(heterocyclic
 amino)-5,6,7,8-tetrahydronaphthal derivatives
 AUTHOR(S): Zhang, Mingli; Shen, Jihua; Wang, Yunling; Yao, Wenli;
 Zhang, Hongbei; Wang, Lihua; Wang, Jian; Li, Fulin
 CORPORATE SOURCE: Inst. Epidemiol. Microbiol., Mil. Acad. Med. Sci.,
 Beijing, Peop. Rep. China
 SOURCE: Yiyao Gongye (1985), 16(2), 56-60
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



I

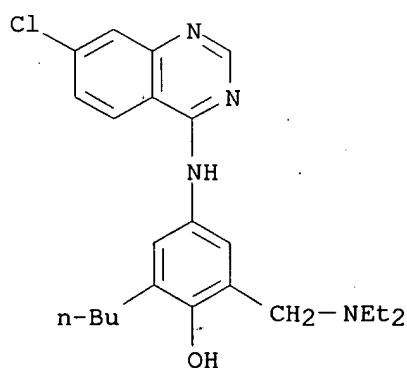
AB Title compds. I [R = (un)substituted heteroaryl, R1 = Et, R12N = pyrrolidino, piperidino, morpholino] were prepared starting from 5,6,7,8-tetrahydronaphthal. I (R = 7-chloro-8-quinolinyl, R12N = pyrrolidino) showed 100% inhibition against chloroquine resistant strain of Plasmodium berghei at 20 mg/kg in mice.

IT 97797-21-2P

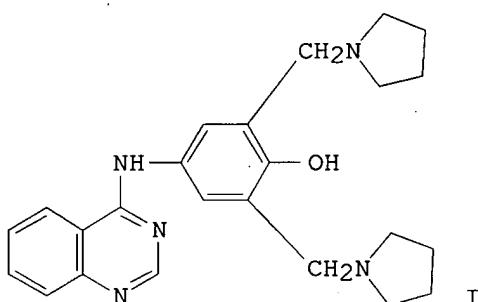
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Préparation)
 (preparation and antimalarial activity of)

RN 97797-21-2 HCPLUS

CN Phenol, 2-butyl-4-[(7-chloro-4-quinazolinyl)amino]-6-[(diethylamino)methyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1985:481478 HCAPLUS
 DOCUMENT NUMBER: 103:81478
 TITLE: Antagonistic effects of changrolin on contraction of rabbit aortic rings evoked by norepinephrine, potassium and calcium
 AUTHOR(S): Li, Hanqing; Chen, Weizhou; Ding, Guangsheng
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, 200031, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1985), 6(2), 93-6
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



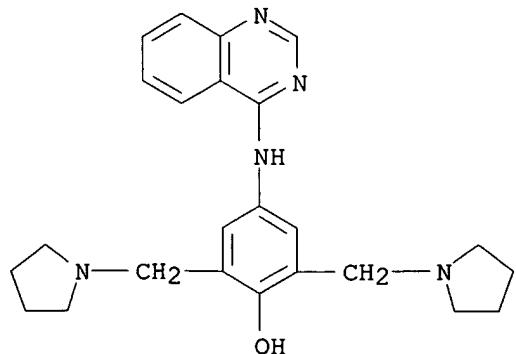
AB The antagonistic effect of changrolin (I) [72063-47-9], a new antiarrhythmic agent, on the contraction of isolated rabbit aortic rings evoked by norepinephrine (0.01-10 nM), KCl (14.7-84.7 mM) and CaCl₂ (0.1-3 mM) was examined. Papaverine, verapamil and phentolamine were used as reference compds. I shifted the cumulative concentration-response curves for norepinephrine, KCl and CaCl₂ to the right and depressed the maximal contraction responses with an IC₅₀ of 0.25, 0.4 and 0.2 mM, resp. As shown by the -log IC₅₀, I effects were similar to those of papaverine but different from those of phentolamine and verapamil. It is suggested that I is not a Ca²⁺ channel blocker.

IT 72063-47-9

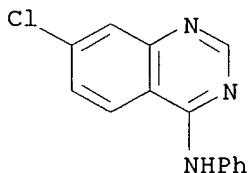
RL: BIOL (Biological study)
 (aorta contraction response to, mechanism of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

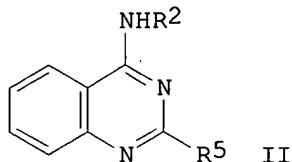
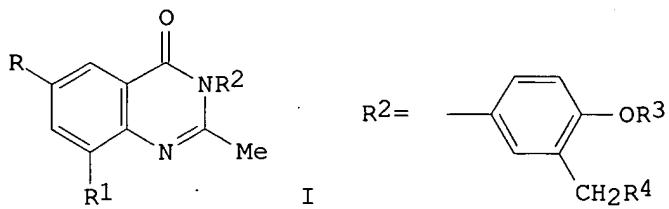


L6 ANSWER 172 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1985:459157 HCPLUS
 DOCUMENT NUMBER: 103:59157
 TITLE: Solubility of basic amino compounds
 AUTHOR(S): Kurihara, Kozo; Otsuka, Yuji
 CORPORATE SOURCE: Prod. Dev. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
 SOURCE: Sankyo Kenkyusho Nenpo (1984), 36, 157-73
 CODEN: SKKNAJ; ISSN: 0080-6064
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Unusual solubility-pH profiles of basic amino compds. and the effect of inorg. salts on the solubility-pH profile were expounded theor. on the basis of solubility product and common-ion effect. The solubility of some basic compound hydrochlorides was theor. dependent on the amount of the solid phase of the basic compds. existing in the system. The theory was confirmed exptl. when 4-anilino-7-chloroquinazoline [74303-34-7] was used as a basic amino compound
 IT 74303-31-4
 RL: BIOL (Biological study)
 (solubility-pH profile of)
 RN 74303-31-4 HCPLUS
 CN 4-Quinazolinamine, 7-chloro-N-phenyl-, monohydrochloride (9CI) (CA. INDEX NAME)



● HCl

L6 ANSWER 173 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1985:203933 HCPLUS
 DOCUMENT NUMBER: 102:203933
 TITLE: Synthesis and antimalarial activity of some new quinazoline derivatives
 AUTHOR(S): Singhal, N.; Gupta, I. S.; Bansal, P. C.
 CORPORATE SOURCE: Dep. Chem. Eng. Technol., Panjab Univ., Chandigarh, 160 014, India
 SOURCE: Journal of the Indian Chemical Society (1984), 61(8), 690-3
 CODEN: JICSAH; ISSN: 0019-4522
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 102:203933
 GI



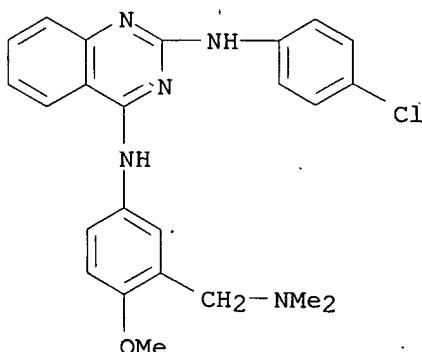
AB Quinazolinones I (R, R1 = H, Cl; R3 = Me, Et; R4 = NMe2, NEt2, piperidino) and quinazolines II (R5 = H, 4-ClC6H4NH, R2) were prepared by aminolysis of benzoxazinones and by substitution on chloroquinazolines. Several of them were tested for antimalarial activity against Plasmodium gallinaceum in chicks and Plasmodium berghei in mice.

IT 96285-09-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and antimalarial activity of)

RN 96285-09-5 HCPLUS

CN 2,4-Quinazolinediamine, N2-(4-chlorophenyl)-N4-[3-[(dimethylamino)methyl]-4-methoxyphenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L6 ANSWER 174 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:142789 HCPLUS

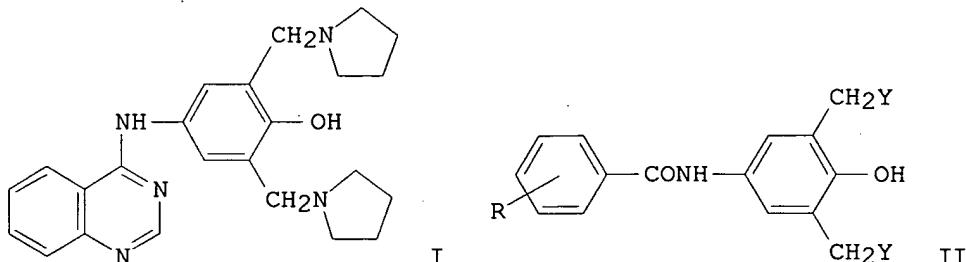
DOCUMENT NUMBER: 102:142789

TITLE: Quantum pharmacological study of the new antiarrhythmic agent Changrolin and its analogs

AUTHOR(S): Wu, Jian; Chen, Kaixian; Ji, Ruyun

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, 200031, Peop. Rep. China

SOURCE: Fenzi Kexue Yu Huaxue Yanjiu (1984), 4(4), 459-64
 CODEN: FKYYDG
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



AB Changrolin (I) [72063-47-9] is a novel antiarrhythmic agent. Various analogs II ($R = H$ or $1,2,3-(OCH_3)_3$; $Y = pyrrolidinyl$, $1-piperidinyl$, or $merpholino$) were synthesized, and their antiarrhythmic activities were evaluated in rodents. The optimization conformation of Changrolin was calculated and the correlation between the pharmacol. effects and EHMO calcns. is discussed.

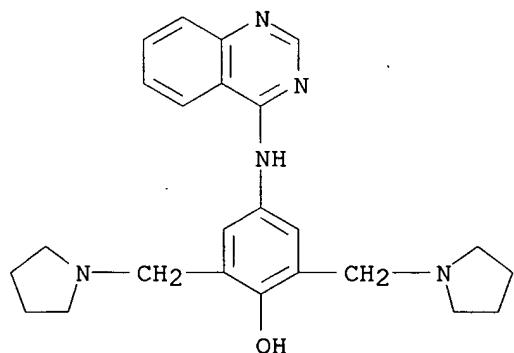
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of, MO in relation to)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 175 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:125059 HCPLUS

DOCUMENT NUMBER: 102:125059

TITLE: Binding of changrolin to plasma and tissue homogenates

AUTHOR(S): Jiang, Jirong; Xu, Guoying; Zeng, Yanlin

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci.,

Shanghai, Peop. Rep. China

SOURCE: Yiyao Gongye (1985), 16(1), 23-5

CODEN: YIGODN; ISSN: 0255-7223

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The binding of the antiarrhythmic drug changrolin [72063-47-9] to plasma was 30.6% in mice, 21.1% in rats, 27.2% rabbits, 39.6% in dogs, and 22.8% in men, while binding to liver, kidney, brain, lung, spleen, and heart homogenates was 55.7, 55.5, 56.4, 51.5, 24.4, and 25.2%, resp. The affinities of changrolin for tissue were usually higher than those for plasma. The binding data obtained with 10, 20, 30, and 60% kidney homogenates were plotted, and the binding by undiluted kidney homogenate was calculated by extrapolation to be 78.4%.

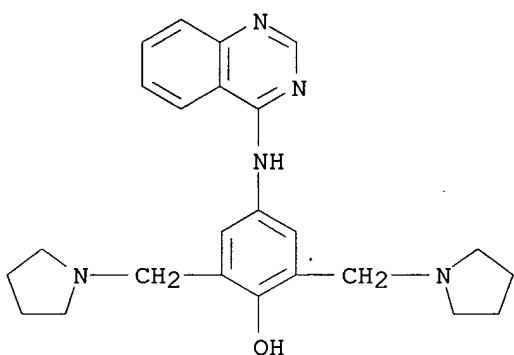
IT 72063-47-9

RL: PROC (Process)

(binding of, by blood plasma and tissue homogenates)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 176 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:24579 HCAPLUS

DOCUMENT NUMBER: 102:24579

TITLE: Preparation of substituted 2-phenyl-4-anilinoquinazolines through imidoylecarbodiimides

AUTHOR(S): Stankovsky, S.; Mrazova, D.

CORPORATE SOURCE: Dep. Org. Chem., Slovak Tech. Univ., Bratislava, CS-812 37, Czech.

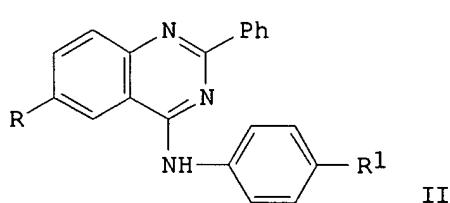
SOURCE: Chemicke Zvesti (1984), 38(4), 549-55

DOCUMENT TYPE: CODEN: CHZVAN; ISSN: 0366-6352

LANGUAGE: English

OTHER SOURCE(S): CASREACT 102:24579

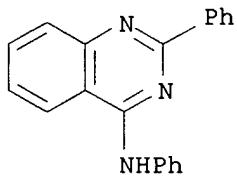
GI



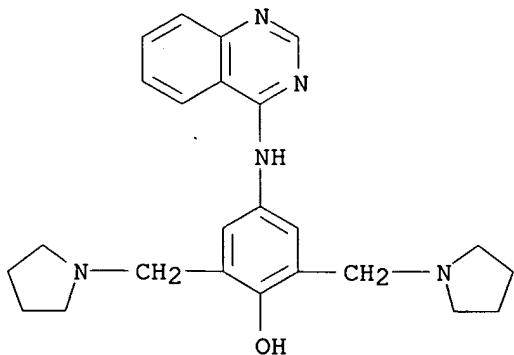
AB 4-RC₆H₄N:CPhNHCSNHC₆H₄R₁-4 (I, R, R₁ = H, Me, Cl) were prepared in 50-70% yields by treating 4-RC₆H₄N:CPhNCS with 4-R₁C₆H₄NH₂. Oxidative cyclization of I with HgO gave 56-68% quinazolines II.

IT 40288-70-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 40288-70-8 HCAPLUS
 CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



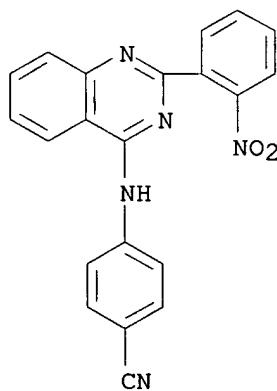
L6 ANSWER 177 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:583742 HCAPLUS
 DOCUMENT NUMBER: 101:183742
 TITLE: Antiarrhythmic effects of changrolin combined with nicotinamide
 AUTHOR(S): Gu, Chonggang; Chen, Weizhou; Dong, Yueli; Ding, Guangsheng
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci.,
 Shanghai, 200031, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1984), 5(3), 173-7
 CODEN: CYLPDN; ISSN: 0253-9756
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB The ED50 of changrolin [72063-47-9] in combination with nicotinamide [98-92-0] against CHCl₃-induced ventricular fibrillation in mice was 3.6 mg/kg, as compared with 9.7 mg/kg for changrolin alone. In beiwutine-induced arrhythmias in rats the antiarrhythmic efficacy of changrolin plus nicotinamide was 69% greater than that of changrolin alone. The effect of changrolin and nicotinamide administered sep. or combined on the ventricular fibrillation threshold to elec. stimulation was examined. An elevation of 0.2 mA was produced by nicotinamide 400 mg/kg i.v., 2.4 mA by changrolin 5 mg/kg i.v., and 4.1 mA by the 2 drugs together.
 IT 72063-47-9
 RL: BIOL (Biological study)
 (heart arrhythmia inhibition by nicotinamide and)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 178 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:551814 HCPLUS
 DOCUMENT NUMBER: 101:151814
 TITLE: Triazines and related products. Part 27. Thermolysis
 of 4-anilino-1,2,3-benzotriazines
 AUTHOR(S): Baig, Ghous Umissa; Stevens, Malcolm F. G.; Vaughan,
 Keith
 CORPORATE SOURCE: Dep. Pharm., Univ. Aston, Birmingham, B4 7ET, UK
 SOURCE: Journal of the Chemical Society, Perkin Transactions
 1: Organic and Bio-Organic Chemistry (1972-1999)
 (1984), (5), 999-1003
 CODEN: JCPRB4; ISSN: 0300-922X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 101:151814
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Thermolysis of benzotriazine I in refluxing morpholine for 7 h gave
 benzotriazine II in addition to the major product, amidine III. The yield of
 II increased in high boiling nonnucleophilic solvents. Decomposition of II in
 hot AcOH gave 4-(4-cyanophenyl)-2-phenylquinazoline derivs.
 IT 92000-85-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydrogenation of)
 RN 92000-85-6 HCPLUS
 CN Benzonitrile, 4-[(2-(2-nitrophenyl)-4-quinazolinyl)amino]- (9CI) (CA
 INDEX NAME)

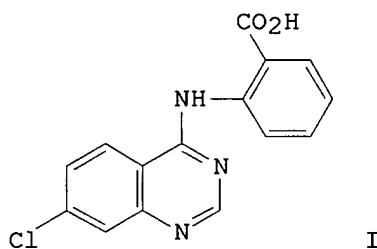


L6 ANSWER 179 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:407190 HCPLUS
 DOCUMENT NUMBER: 101:7190
 TITLE: 2-(7-Chloro-4-quinazolyl)aminobenzoic acid
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 2 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|----------|----------|-----------------|----------|
| JP 59013765 | A | 19840124 | JP 1982-123215 | 19820715 |
| JP 03078384 | B | 19911213 | | |
| PRIORITY APPLN. INFO.: | | | JP 1982-123215 | 19820715 |
| OTHER SOURCE(S): | CASREACT | 101:7190 | | |
| GI | | | | |



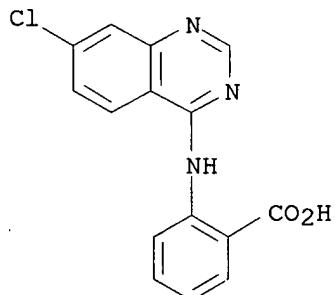
AB Title compound (I), having analgesic, antipyretic, and antiinflammatory activities (no data), was prepared by reaction of 4,7-dichloroquinazoline (II) with 2-H₂NC₆H₄CO₂H (III). Thus, 4 g II was added to a mixture of 1.3 g KOH and 3.4 g III in MeOH and the whole refluxed 1 h to give 83.3% I.

IT 90430-16-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 90430-16-3 HCAPLUS

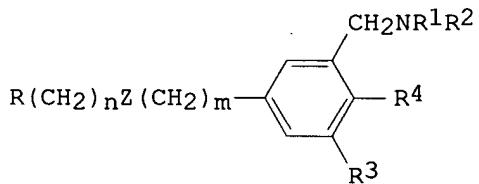
CN Benzoic acid, 2-[(7-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 180 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:406802 HCAPLUS
 DOCUMENT NUMBER: 101:6802
 TITLE: Heteroaryl substituted aminomethylbenzene derivatives,
 compositions and use
 INVENTOR(S): Stout, David M.; Matier, William L.
 PATENT ASSIGNEE(S): American Hospital Supply Corp., USA
 SOURCE: PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------------------------------------|----------|-----------------|-------------|
| WO 8400489 | A1 | 19840216 | WO 1983-US1103 | 19830718 |
| W: AU, JP, NO
RW: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| US 4466965 | A | 19840821 | US 1982-401752 | 19820726 |
| AU 8318299 | A | 19840223 | AU 1983-18299 | 19830718 |
| AU 568087 | B2 | 19871217 | | |
| ZA 8305224 | A | 19840328 | ZA 1983-5224 | 19830718 |
| JP 59501318 | T | 19840726 | JP 1983-502675 | 19830718 |
| EP 114878 | A1 | 19840808 | EP 1983-902608 | 19830718 |
| EP 114878 | B1 | 19900926 | | |
| R: BE, CH, DE, FR, GB, LI, LU, NL, SE | | | | |
| EP 310155 | A1 | 19890405 | EP 1988-201796 | 19830718 |
| R: BE, CH, DE, FR, GB, LI, LU, NL, SE | | | | |
| ES 524447 | A1 | 19841201 | ES 1983-524447 | 19830726 |
| CA 1240996 | A1 | 19880823 | CA 1983-433226 | 19830726 |
| NO 8401192 | A | 19840326 | NO 1984-1192 | 19840326 |
| NO 162466 | B | 19890925 | | |
| NO 162466 | C | 19900110 | | |
| US 4666924 | A | 19870519 | US 1984-617286 | 19840604 |
| US 4923873 | A | 19900508 | US 1987-50354 | 19870518 |
| PRIORITY APPLN. INFO.: | | | US 1982-401752 | A 19820726 |
| | | | EP 1983-902608 | P 19830718 |
| | | | WO 1983-US1103 | A 19830718 |
| | | | US 1984-617286 | A3 19840604 |
| OTHER SOURCE(S): | CASREACT 101:6802; MARPAT 101:6802 | | | |
| GI | | | | |



AB Title compds. I [n and m are 0,1,2,3,4,5; R = fused or unfused six-membered N heterocycle; R1 and R2 are H, alkyl, hydroxyalkyl, cycloalkyl, alkoxyalkyl, alkoxyaryl, aryl, heteroaryl, or NR1R2 form a heterocycle; R3 = H, CH2NR1R2; R4 = H, OH, NH2, acyloxy, alkoxy, alkanesulfonamido, aralkoxy; Z = NR5 (R5 = H, aryl, alkyl), CONR5, NR5CO, C(O)O, OC(O), O, CO, alkylene, S], which were prepared, showed antiarrhythmic and anticholinergic activity. Thus, 4-H2NC6H4OH was N-arylated by 1-chlorophthalazine, and the product was treated with HCHO and pyrrolidine to give I (R = 1-phthalazinyl, Z = NH, n = m = 0, NR1R2 = pyrrolidino, R3 = pyrrolidinomethyl, R4 = OH).

IT 90446-33-6P

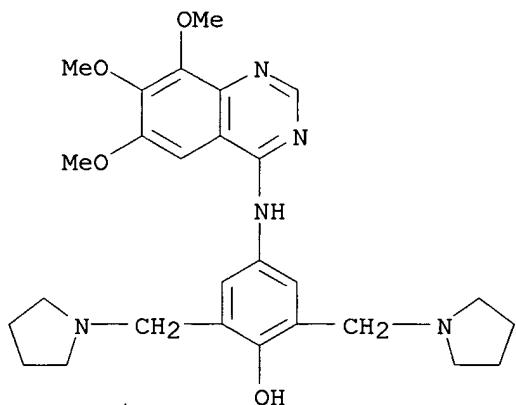
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and pharmacol. activity of)

RN 90446-33-6 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-[(6,7,8-trimethoxy-4-

(quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 181 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:167971 HCAPLUS

DOCUMENT NUMBER: 100:167971

TITLE: Effects of changrolin on contractility and excitability of cat myocardium papillary muscle

AUTHOR(S): Li, Ruisong; Chen, Weizhou; Zhang, Yuefang; Ding, Guangsheng

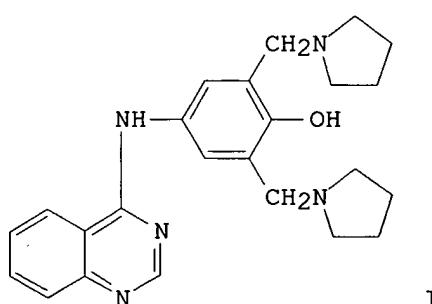
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, 200031, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1984), 5(1), 26-9
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



I

AB The neg. inotropic effect of changrolin (I) [72063-47-9] in isolated cat papillary muscles was completely antagonized by nicotinamide and isoproterenol. Simultaneous addition of I and CaCl₂ to the preps. caused intermittent or complete inhibition of contractions. Nicotinamide and CaCl₂ enhanced the I-induced shift of the intensity-duration curve upward.

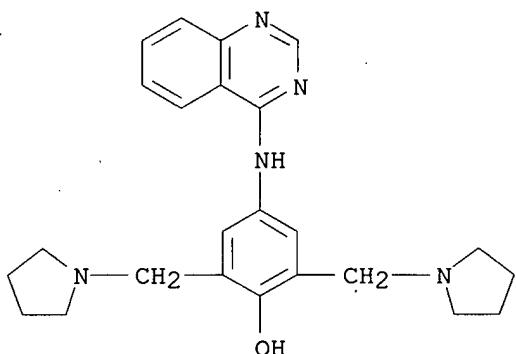
IT 72063-47-9

RL: BIOL (Biological study)
(heart contractility and excitability response to)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA)

INDEX NAME)



L6 ANSWER 182 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:132553 HCPLUS

DOCUMENT NUMBER: 100:132553

TITLE: Selective inhibitors of three forms of cyclic nucleotide phosphodiesterase - basic and potential clinical applications

AUTHOR(S): Hidaka, Hiroyoshi; Endo, Toyoshi

CORPORATE SOURCE: Sch. Med., Mie Univ., Edobashi, 514, Japan

SOURCE: Advances in Cyclic Nucleotide and Protein Phosphorylation Research (1984), 16, 245-59

CODEN: ACNREY; ISSN: 0747-7767

DOCUMENT TYPE: Journal

LANGUAGE: English

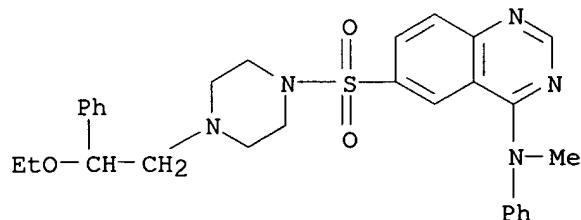
AB Human platelets contain 3 distinct forms of cyclic nucleotide phosphodiesterase (PDE) which can be separated by DEAE-cellulose inhibitors on the function of various tissues (platelets, blood vessels, etc.) is dependent on both the tissue distribution of drugs and each form of PDE. It appears that multiforms of PDE are present in various amounts. in the tissue. A specific inhibitor for each form of PDE could pave the way for basic research on PDE regulation and provide for eventual therapeutic application to control abnormal function.

IT 81871-31-0

RL: BIOL (Biological study)
(cyclic nucleotide phosphodiesterase inhibition by)

RN 81871-31-0 HCPLUS

CN Piperazine, 1-(2-ethoxy-2-phenylethyl)-4-[[4-(methylphenylamino)-6-quinazolinyl]sulfonyl]- (9CI) (CA INDEX NAME)

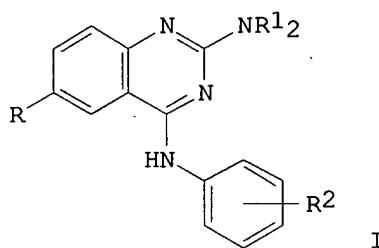


L6 ANSWER 183 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

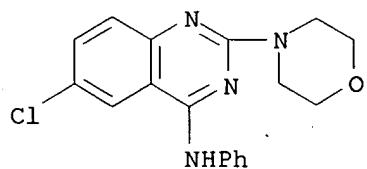
ACCESSION NUMBER: 1984:121013 HCPLUS

DOCUMENT NUMBER: 100:121013

TITLE: Reactions of amidinoyl isothiocyanates with
 N-sulfinylanilines
 AUTHOR(S): Stankovsky, S.; Burkova, V.
 CORPORATE SOURCE: Dep. Org. Chem., Slovak Tech. Univ., Bratislava, 812
 37, Czech.
 SOURCE: Chemicke Zvesti (1983), 37(6), 831-6
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 100:121013
 GI



AB p-RC₆H₄N:C(NR₁₂)N:C:S (R = H, Cl, Br; R₁ = Et, R₁₂N = morpholino, 4-phenylpiperazino) underwent cyclization with R₂C₆H₄N:S:O (R₂ = p-O₂N, o-O₂N, p-Me, H) to give anilinoquinazolines I in 21-44% yield.
 IT 60973-41-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 60973-41-3 HCPLUS
 CN 4-Quinazolinamine, 6-chloro-2-(4-morpholinyl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 184 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:34492 HCPLUS
 DOCUMENT NUMBER: 100:34492
 TITLE: The synthesis of some quinazoline derivatives and
 their biological properties
 AUTHOR(S): Karminski, W.; Kulicka, J.; Miernik, J.
 CORPORATE SOURCE: Inst. Org. Chem. Technol., Silesian Polytech. Univ.,
 Gliwice, Pol.
 SOURCE: Journal of Environmental Science and Health, Part B:
 Pesticides, Food Contaminants, and Agricultural Wastes
 (1983), B18(4-5), 599-610
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 CODEN: JPFCD2; ISSN: 0360-1234

OTHER SOURCE(S): CASREACT 100:34492

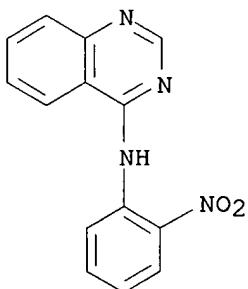
AB Fifteen 4-substituted-, 7 2,4-disubstituted-, and 5 2,4,6,8-tetrasubstituted-quinazolines were prepared and tested for herbicidal, insecticidal, acaricidal, and fungicidal activity. All were ineffective except for 4-chloroquinazoline, which showed mild fungicidal activity.

IT 88404-42-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and herbicidal-insecticidal activities of)

RN 88404-42-6 HCPLUS

CN 4-Quinazolinamine, N-(2-nitrophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 185 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:594917 HCPLUS

DOCUMENT NUMBER: 99:194917

TITLE: Reactions with 4-[p-(substituted cinnamoyl)anilino]-2-phenylquinazolines

AUTHOR(S): Mahmoud, A. M.; El-Sherief, H. A. H.; Esmaiel, A. A.

CORPORATE SOURCE: Fac. Sci., Assiut Univ., Assiut, Egypt

SOURCE: Acta Chimica Hungarica (1983), 113(3), 247-56

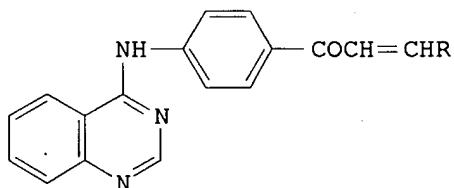
CODEN: ACHUDC; ISSN: 0231-3146

DOCUMENT TYPE: Journal

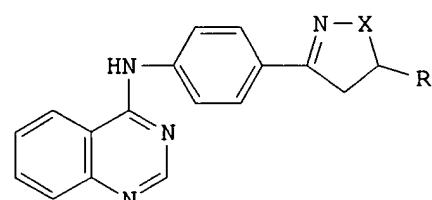
LANGUAGE: English

OTHER SOURCE(S): CASREACT 99:194917

GI



I



II

AB Chalcone analogs I [R = (un)substituted Ph, 1-C₁₀H₇, 2-furyl, 2-thienyl], prepared in 68-85% yields by condensation of RCHO with the corresponding acetophenone derivative, were cyclocondensed with N₂H₄.H₂O, PhNNHNH₂, and

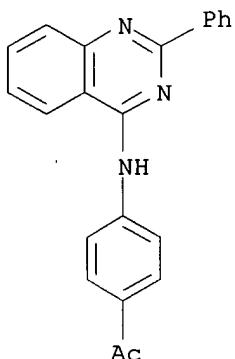
NH₂OH.HCl to give 60-75% and 69-80%, resp., of II [X = NR₁ (R₁ = H, Ph); R = p-BrC₆H₄, p-ClC₆H₄, p-MeOC₆H₄, p-Me₂NC₆H₄] and III (X = O, R = p-ClC₆H₄, p-MeOC₆H₄, p-Me₂NC₆H₄). Addnl. products were obtained from I by bromination and subsequent substitution reactions and by cyclocondensation with MeCOCH₂CO₂Et.

IT 87771-83-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with aldehydes)

RN 87771-83-3 HCPLUS

CN Ethanone, 1-[4-[(2-phenyl-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 186 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:587363 HCPLUS

DOCUMENT NUMBER: 99:187363

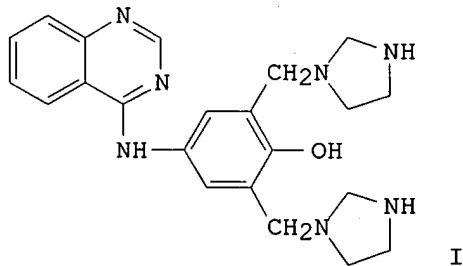
TITLE: Effect of changrolin on the action potential of canine Purkinje fibers

AUTHOR(S): Gu, Peikun; Wang, Binyao; Chen, Yanlian; Shang, Ming;
Liu, Xueji; Jin, ZhengjunCORPORATE SOURCE: Dep. Pharmacol., Shanghai 2nd. Med. Coll., Shanghai,
200025, Peop. Rep. ChinaSOURCE: Zhongguo Yaoli Xuebao (1983), 4(3), 170-2
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

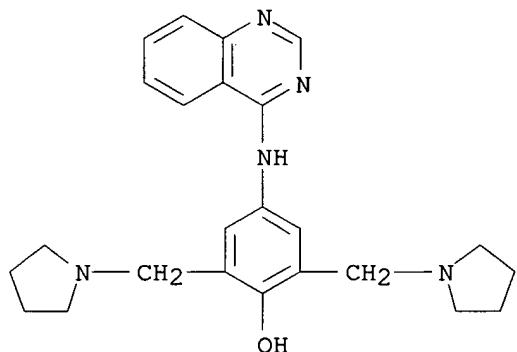
LANGUAGE: Chinese

GI

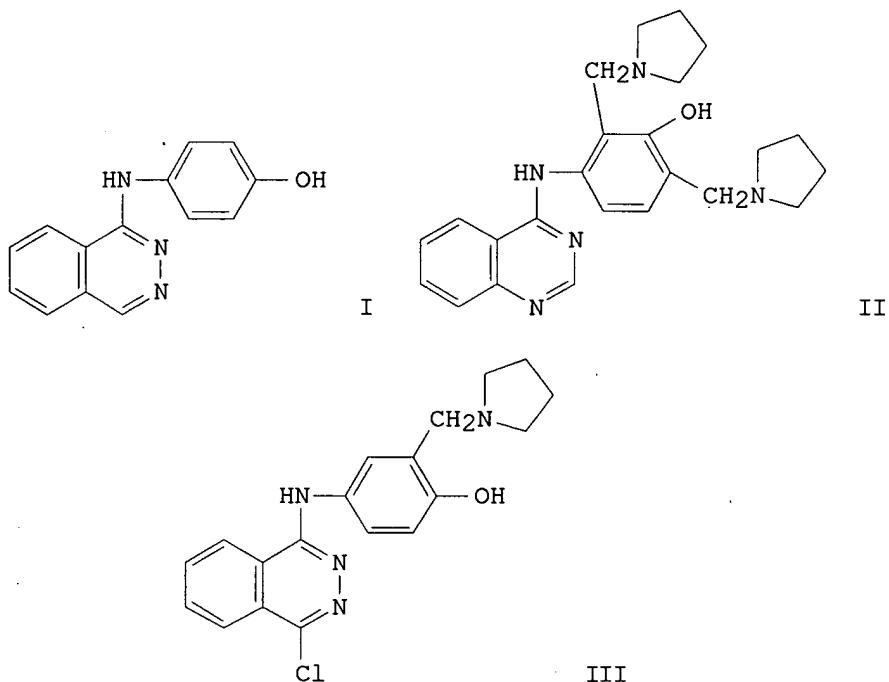


AB Changrolin (I) [72063-47-9] reversibly lengthened the action potential duration and effective refractory period of canine Purkinje fibers; it also suppressed an elec. evoked arrhythmia.
IT 72063-47-9

RL: BIOL (Biological study)
(heart arrhythmia and Purkinje fiber elec. activity response to)
RN 72063-47-9 HCPLUS
CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA
INDEX NAME)



L6 ANSWER 187 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:198131 HCPLUS
DOCUMENT NUMBER: 98:198131
TITLE: Synthesis and antiarrhythmic and parasympatholytic properties of substituted phenols. 1.
Heteroarylamine derivatives
AUTHOR(S): Stout, David M.; Matier, W. L.; Barcelon-Yang, Cynthia; Reynolds, Robert D.; Brown, Barry S.
CORPORATE SOURCE: Sect. Med./Org. Chem., Am. Hosp. Supply Corp., McGraw Park, IL, 60085, USA
SOURCE: Journal of Medicinal Chemistry (1983), 26(6), 808-13
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



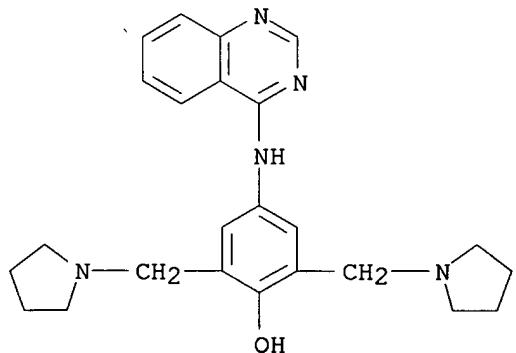
AB Twenty-four structural derivs., e.g. I, II, and III, of the antiarrhythmic drug changrolin were prepared and tested for antiarrhythmic and parasympatholytic activities. Thus, treating 1-chlorophthalazine with p-H₂NC₆H₄OH gave I. Although the bis(pyrrolidinyl)methylphenol pattern of changrolin seemed optimal in this series, a wide latitude existed for the heteroaryl substituent for maintaining good antiarrhythmic activity. The antiarrhythmic and parasympatholytic activities tended to exhibit parallel changes.

IT 72063-47-9

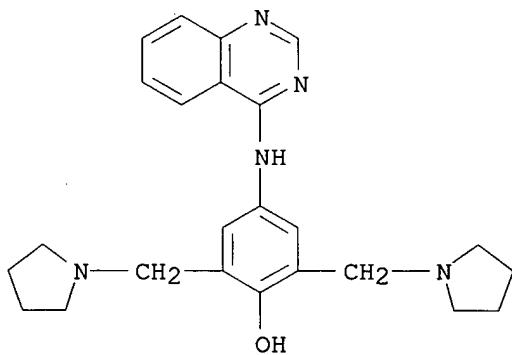
RL: RCT (Reactant); RACT (Reactant or reagent)
(antiarrhythmic and parasympatholytic activity of analogs of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 98:191531
 TITLE: Effect of K-strophanthin or adoniside in combination with antiarrhythmic drugs on aconitine induced cardiac arrhythmia in mice
 AUTHOR(S): Shen, Xiaotong; Qian, Yaoxian; Wang, Shengben; Lin, Jiabao; Ding, Jianmi; Yang, Zaochen
 CORPORATE SOURCE: Fac. Basic Med. Sci., Shanghai First Med. Coll., Shanghai, Peop. Rep. China
 SOURCE: Shanghai Diyi Yixueyuan Xuebao (1983), 10(1), 41-6
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 AB k-strophanthin (I) [11005-63-3] not only possessed an antiarrhythmic action, but also potentiated the antiarrhythmic action of changrolin [72063-47-9] and propranolol [525-66-6]. Furthermore, when I was used in combination with lidocaine [137-58-6], phenytoin [57-41-0] or bretylium [59-41-6], the antiarrhythmic action appeared to be additive. Although adoniside [8002-00-4] was unable to prolong the latent period of cardiac arrhythmia it could potentiate the antiarrhythmic action of disopyramide [3737-09-5]. The antiarrhythmic actions of disopyramide and changrolin were also shown to be additive.
 IT 72063-47-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiarrhythmic activity of, strophanthin potentiation of)
 RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 189 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1983:143349 HCAPLUS
 DOCUMENT NUMBER: 98:143349
 TITLE: Some reactions of 3-[2'-(4'H,2',1')-benzoxazin-4'-onyl]coumarins and 3-(2'-quinazol-4'-onyl)coumarins
 AUTHOR(S): El-Hashash, M. A.; Kaddah, A. M.; El-Kady, M.; Ammer, M. M.
 CORPORATE SOURCE: Fac. Sci., Ain Shams Univ., Cairo, Egypt
 SOURCE: Pakistan Journal of Scientific and Industrial Research (1982), 25(4), 104-8
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 98:143349
 GI

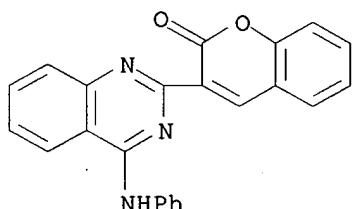
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Condensation of benzoxazinylcoumarins I ($R = H, Br; X = O$) with NH_4OAc or $HCONH_2$ at 190° gave I ($X = NH$). Treatment of I ($R = H, X = NH$) with $BzCl$ or $POCl_3$ gave quinazolinylcoumarins II ($R_1 = BzO, Cl$), and ring cleavage of I ($X = O$) with anilines gave coumarincarboxanilides III ($R_2 = Me, Cl, CO_2H$). Condensation of I ($X = O, NH$) with N_2H_4 gave salicylaldehyde azines and the pyrazolinone IV, and Michael addition of I ($R = H, X = O$) with $MeCOCH_2CO_2Et$ gave pyranobenzopyrandione V whereas addition with $MeCOCH_2COMe$ gave dihydrocoumarin VI. Cyclocondensation of NaN_3 and I ($R = H, X = O$) gave tetrazole VII.

IT 85226-80-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 85226-80-8 HCPLUS

CN 2H-1-Benzopyran-2-one, 3-[4-(phenylamino)-2-quinazolinyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 190 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:89384 HCPLUS

DOCUMENT NUMBER: 98:89384

TITLE: 4-Anilinoquinazoline derivatives

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.

CODEN: JKXXAF

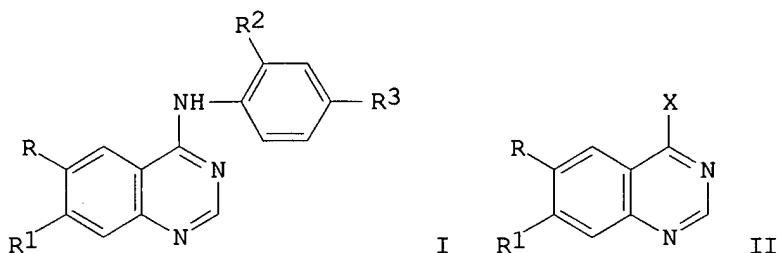
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|----------|----------|-----------------|----------|
| JP 57144266 | A | 19820906 | JP 1981-30816 | 19810304 |
| PRIORITY APPLN. INFO.: | | | JP 1981-30816 | 19810304 |
| OTHER SOURCE(S): | CASREACT | 98:89384 | | |
| GI | | | | |



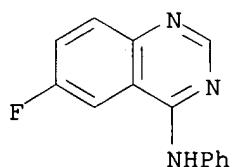
AB 4-Anilinoquinazoline derivs. I ($R, R1, R2, R3 = F, H, H, H; F, H, Me, Me; F, H, H, Et; F, H, OMe; F, H, H, F; H, F, H, Et; H, F, H, F$) were prepared by reaction of II ($X = \text{halo}$) with $2,4\text{-R}2\text{R}3\text{C}6\text{H}3\text{NH}2$. Analgesic and antiinflammatory data of I were shown in rats by the Randall-Selitto method and the carrageenin edema method, resp. Thus, heating 3.6 g II ($R = F, R1 = H, X = \text{Cl}$) with $\text{PhNH}2$ in EtOH 5' min gave 73% I ($R = F, R1 = R2 = R3 = H$).

IT 84729-27-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic and antiinflammatory activity of)

RN 84729-27-1 HCPLUS

CN 4-Quinazolinamine, 6-fluoro-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 191 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:574781 HCPLUS

DOCUMENT NUMBER: 97:174781

TITLE: Effects of changrolin and pyracrine phosphate on ATPase of rabbit heart sarcolemma

AUTHOR(S): Chen, Enhong; Tu, Zenghong; Yang, Huihua; Wu, Weiwei
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chinese Acad. Sci.,

Shanghai, Peop. Rep. China

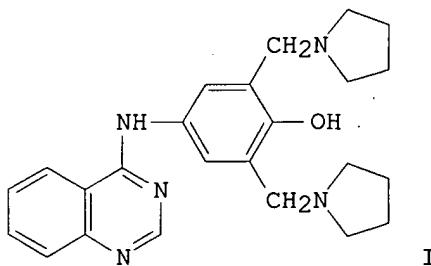
SOURCE: Zhongguo Yaoli Xuebao (1982), 3(3), 183-5

CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



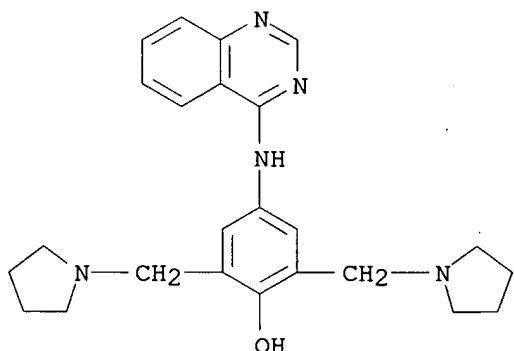
AB The inhibitory effects of changrolin (I) [72063-47-9] and quinidine [56-54-2] (1 mM) on the Na⁺,K⁺-ATPase [9000-83-3] activity of rabbit heart sarcolemma were 24% and 50%, resp. The inhibitory effects of pyracrine phosphate (II) [76975-05-8] and mepacrine [83-89-6] on Na⁺, K⁺-ATPase were more potent. The inhibitory effect of pyracrine phosphate was similar to that of ouabain. The effects of changrolin and pyracrine phosphate on Ca²⁺-ATPase activity were not significant at 0.5 and 1 mM.

IT 72063-47-9

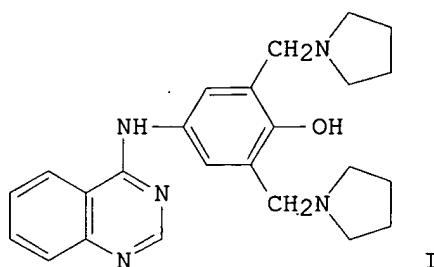
RL: BIOL (Biological study)
(ATPase of heart sarcolemma response to, pyracrine phosphate in relation to)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 192 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:574778 HCAPLUS
 DOCUMENT NUMBER: 97:174778
 TITLE: Effect of antiarrhythmic drug changrolin on fast and slow response potentials of myocardial cell of rats
 AUTHOR(S): Li, Zhenyuan
 CORPORATE SOURCE: Dep. Physiol., Zhejiang Med. Univ., Hangzhou, Peop. Rep. China
 SOURCE: Zhongguo Yaoli Xuebao (1982), 3(3), 172-5
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



AB The effects of changrolin (I) [72063-47-9] on the normal fast action potential and the evoked slow response of ventricular cells were studied in vitro using an intracellular capillary glass electrode. The amplitude and maximal depolarization rate of phase 0 (Vmax) of the fast action potential were decreased, the duration of the action potential shortened, the effective refractory period prolonged, and the excitability decreased, but the resting potential remained practically unchanged. For the slow response, the amplitude, depolarization rate of the action potential and especially the effective refractory period were increased, and the duration of the action potential was prolonged after changrolin administration. Apparently, changrolin may be a new type of antiarrhythmic drug.

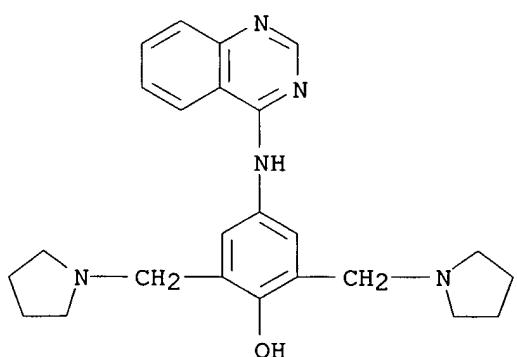
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 193 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:455767 HCPLUS

DOCUMENT NUMBER: 97:55767

TITLE: Some reactions of 4-chloroquinazoline, 6-nitro- and 6-amino-4(3H)-quinazolones

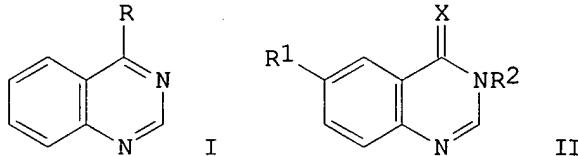
AUTHOR(S): Anwar, M.; Abdel-Hay, F. I.; Elbarbary, A. A.; El-Borai, M.

CORPORATE SOURCE: Fac. Sci., Tanta Univ., Tanta, Egypt

SOURCE: Revue Roumaine de Chimie (1981), 26(11-12), 1469-78

CODEN: RRCHAX; ISSN: 0035-3930

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 97:55767
 GI

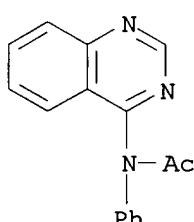


AB Quinazolines I [R = NHCONH₂, NHCHO, NHAc, NAcPh, NAcC₆H₄Me-2, NAcC₆H₄Me-4, N-acetyl-N-1-naphthylamino, NHNC₆H₄NO₂-4, NHNC₆H₃(NO₂)₂-2, 4] were prepared by aminating I (R = Cl). II (X = O, S; R₁ = H, NO₂; R₂ = aminomethyl) were obtained by aminomethylating II (R₂ = H). III (X = O, R₁ = NH₂, R₂ = H) was treated with MeCOCH₂CO₂Et to give III (X = O, R₁ = NHCOCH₂COMe, R₂ = H) which was treated with 4-R₃C₆H₄N₂⁺ (R₃ = H, Me, OMe) to give III [X = O, R₁ = 4-R₃C₆H₄N:NC(:CMeOH)CONH, R₂ = H].

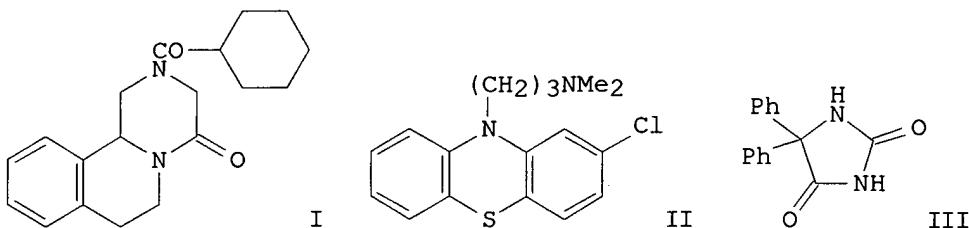
IT 82436-00-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 82436-00-8 HCPLUS

CN Acetamide, N-phenyl-N-4-quinazolinyl- (9CI) (CA INDEX NAME)



L6 ANSWER 194 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:416857 HCPLUS
 DOCUMENT NUMBER: 97:16857
 TITLE: Heart rhythm disturbance in rabbits induced by pyquiton and its treatment and prevention by drugs
 AUTHOR(S): Shao, Baoruo; Xiao, Shuhua; Wu, Huimin; Zhan, Chongqing
 CORPORATE SOURCE: Inst. Parasitic Dis., Chinese Acad. Med. Sci., Shanghai, Peop. Rep. China
 SOURCE: Yaoxue Xuebao (1981), 16(6), 407-10
 CODEN: YHHPAL; ISSN: 0513-4870
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



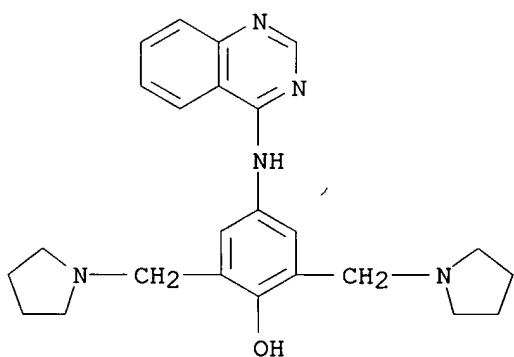
AB Heart arrhythmias developed in apprx. 80% of rabbits given pyquiton (I) [55268-74-1] (35-45 mg/kg, i.v.). The antiarrhythmics phenoxybenzamine [59-96-1] (3 mg/kg), chlorpromazine (II) [50-53-3] (5 mg/kg), isoptin [152-11-4] (0.3-0.5 mg/kg), promethazine [60-87-7] (3-5 mg/kg), and phenytoin (III) [57-41-0] (50 mg/kg) abolished the existing arrhythmias, with phenoxybenzamine being the most effective. Lidocaine [137-58-6], quinidine [56-54-2], isoprenaline [7683-59-2], and atropine [51-55-8] were partially effective, and practolol [6673-35-4] and changrolin [72063-47-9] were inactive. Prior administration of II and III prevented the development of arrhythmias from I.

IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heart arrhythmia from pyquiton prevention and therapy by)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 195 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:416835 HCAPLUS

DOCUMENT NUMBER: 97:16835

TITLE: Comparison of antiarrhythmic effects of intravenous injections of changrolin and BL-4712A

AUTHOR(S): Wang, Changgen; Wang, Zhimin; Zhang, Yuefang; Ding, Guangsheng

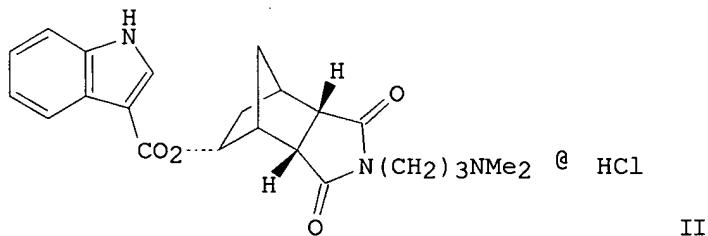
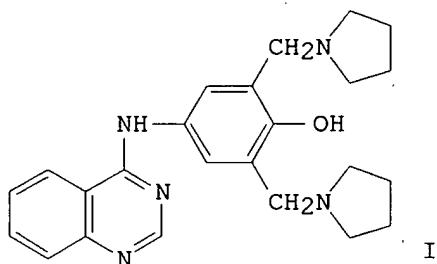
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chinese Acad. Sci.,
Shanghai, 200031, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1982), 3(1), 29-31
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



AB changrolin (I) [72063-47-9] was potent and antiarrhythmic than BL-4712A (II) [59496-26-3] in various exptl. models when given i.v. at equitoxic doses. The acute i.p. LD₅₀ values in mice of I and II were 342 and 83 mg/kg, resp. Equitoxic doses were the same fraction of LD₅₀ for each compound

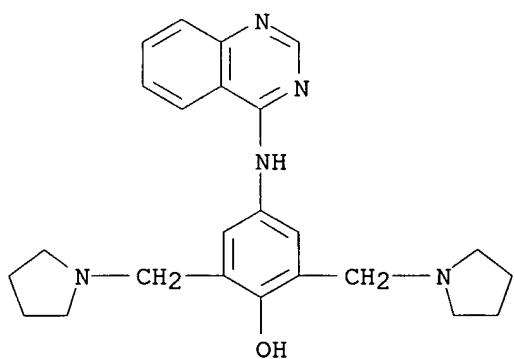
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 196 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:217873 HCPLUS

DOCUMENT NUMBER: 96:217873

TITLE: 6-Quinazolinesulfonyl derivatives

INVENTOR(S): Hidaka, Hiroyoshi; Sone, Takanori; Sasaki, Yasuharu; Sugihara, Taisuke; Takagi, Seiji; Sako, Kiyohide

PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 54 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

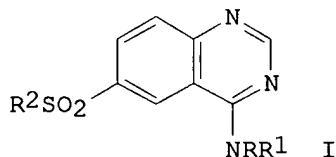
English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------------------------------------|----------|-----------------|------------|
| EP 46572 | A2 | 19820303 | EP 1981-106461 | 19810819 |
| EP 46572 | A3 | 19820714 | | |
| EP 46572 | B1 | 19841031 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| JP 57038775 | A | 19820303 | JP 1980-113401 | 19800820 |
| JP 01038784 | B | 19890816 | | |
| JP 57040474 | A | 19820306 | JP 1980-114658 | 19800822 |
| JP 01038109 | B | 19890811 | | |
| JP 57126482 | A | 19820806 | JP 1981-10847 | 19810129 |
| JP 02027344 | B | 19900615 | | |
| US 4510307 | A | 19850409 | US 1981-293192 | 19810817 |
| PRIORITY APPLN. INFO.: | | | JP 1980-113401 | A 19800820 |
| | | | JP 1980-114658 | A 19800822 |
| | | | JP 1981-10847 | A 19810129 |
| OTHER SOURCE(S): | CASREACT 96:217873; MARPAT 96:217873 | | | |
| GI | | | | |



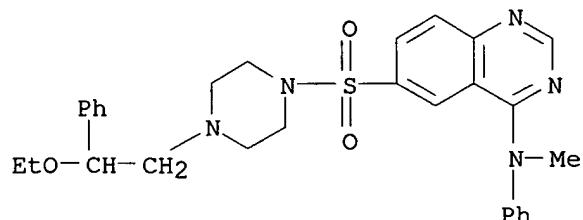
AB Quinazolines I [R = H, alkyl; R1 = H, alkyl, cycloalkyl, aryl; NRR1 = heterocyclic; R2 = 4-substituted piperazino, NH(CH2)nNH2; n = 2-10] were prepared. Thus 4-piperidinoquinazoline was treated with ClSO3H and the resulting 4-piperidino-6-quinazolinylsulfonyl chloride was treated with H2N(CH2)4NH2 to give I [NRR1 = piperidino, R2 = NH(CH2)4NH2] which had a vasodilator ED50 of 21 μmoles in vitro.

IT 81871-31-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and vasodilator and antihypertensive activity of)

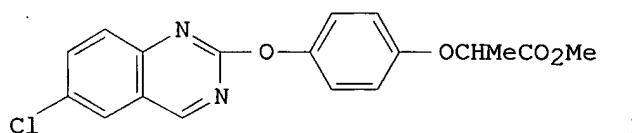
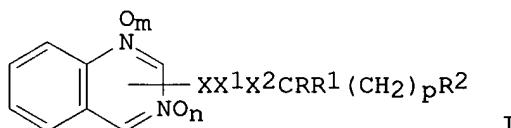
RN 81871-31-0 HCPLUS

CN Piperazine, 1-(2-ethoxy-2-phenylethyl)-4-[4-(methylphenylamino)-6-quinazolinylsulfonyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1982:181301 HCPLUS
 DOCUMENT NUMBER: 96:181301
 TITLE: Quinazolinylloxy(amino)phenoxyalkane carboxylic acid derivatives, herbicidal compositions containing them and their use
 INVENTOR(S): Serban, Alexander; Jensen, Wendy Anne
 PATENT ASSIGNEE(S): ICI Australia Ltd., Australia
 SOURCE: Eur. Pat. Appl., 51 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------|------|----------|-----------------|------------|
| EP 44163 | A2 | 19820120 | EP 1981-302941 | 19810629 |
| EP 44163 | A3 | 19820331 | | |
| R: BE, CH, DE, FR, GB, IT, NL | | | | |
| US 4675047 | A | 19870623 | US 1981-274165 | 19810616 |
| ZA 8104225 | A | 19820929 | ZA 1981-4225 | 19810622 |
| CA 1140128 | A1 | 19830125 | CA 1981-380648 | 19810626 |
| JP 57046969 | A | 19820317 | JP 1981-103142 | 19810701 |
| JP 05007385 | B | 19930128 | | |
| JP 05039273 | A | 19930219 | JP 1991-250096 | 19910626 |
| JP 06104662 | B | 19941221 | | |
| PRIORITY APPLN. INFO.: | | | AU 1980-4318 | A 19800701 |
| GI | | | | |



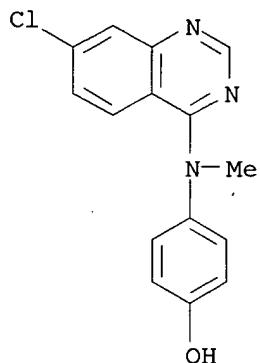
AB The title compds. I [X = O, S, (un)substituted NH; X1 = (un)substituted C6H4; X2 = O, S; R = H, (un)substituted alkyl, Ac, COEt, alkoxy carbonyl; R1 = H, (un)substituted alkyl; RR1 = (CH2)1-3, CMe2; R2 = cyano, CSNH2, CO2H, esterified or amidated CO2H; m, n = 0, 1; p = 0-2; the quinazoline system may be further substituted] were prepared. Thus 2,6-dichloroquinazoline was treated with 4-HOC6H4OCHMeCO2Me to give II which was herbicidal at 2 kg/ha preemergence.

IT 81585-61-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, with bromopropionate)

RN 81585-61-7 HCPLUS

CN Phenol, 4-[(7-chloro-4-quinazolinyl)methylamino]- (9CI) (CA INDEX NAME)



L6 ANSWER 198 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:122738 HCAPLUS

DOCUMENT NUMBER: 96:122738

TITLE: Phosphoramides. XVII. A new synthesis of quinazolinamines

AUTHOR(S): Nielsen, Knud Erik; Pedersen, Erik B.

CORPORATE SOURCE: Dep. Chem., Odense Univ., Odense, DK-5230, Den.

SOURCE: Chemica Scripta (1981), 18(5), 242-4

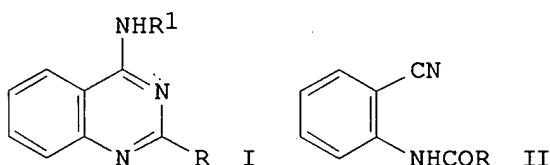
CODEN: CSRPB9; ISSN: 0004-2056

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 96:122738

GI



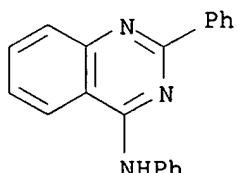
AB Quinazolinamines I ($R = Me, Me_3C, Ph; R_1 = Me, Pr, EtCHMe, Ph$) were prepared in 12-81% yield by heating acylaminobenzonitriles II in a reagent mixture of P_2O_5 , an amine hydrochloride, and N,N -dimethylcyclohexylamine at $180-240^\circ$. In that reagent mixture I could also be obtained by heating $2-H_2NC_6H_4CN$ together with an acylating reagent which could be $HCO_2(CH_2)_4Me$, $HCONEt_2$, or $BzOH$.

IT 40288-70-8P

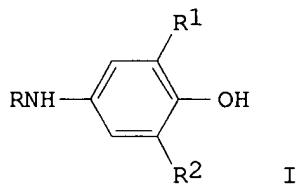
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 40288-70-8 HCAPLUS

CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 199 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:122728 HCPLUS
 DOCUMENT NUMBER: 96:122728
 TITLE: Studies on antiarrhythmics - synthesis of
 2-[(alkylamino)methyl]- and 2,6-
 bis[(alkylamino)methyl]-4-(substituted amino)phenols
 AUTHOR(S): Lin, Mulan; Liu, Yufeng; Lu, Yongyu; Zhang, Huiqin;
 Zheng, Weimin
 CORPORATE SOURCE: Tianjin Inst. Pharm. Ind. Res., Tianjin, Peop. Rep.
 China
 SOURCE: Yaoxue Xuebao (1981), 16(10), 757-61
 DOCUMENT TYPE: CODEN: YHHPAL; ISSN: 0513-4870
 LANGUAGE: Journal
 GI Chinese



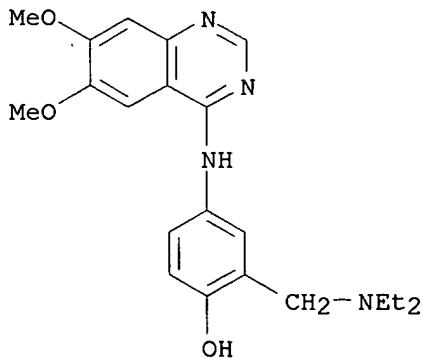
AB 4-Aminophenols I [R = Ac, 2,6-diamino(or dimethyl)-4-pyrimidinyl,
 1-phthalazinyl, 6,7-dimethoxy-4-quinazolinyl, etc.; R1, R2 = H, Et₂NCH₂,
 1-pyrrolidinylmethyl, piperidinomethyl, morpholinomethyl] (37 compds.)
 were prepared by known reactions. Some I showed antiarrhythmic activity.

IT 81080-33-3P

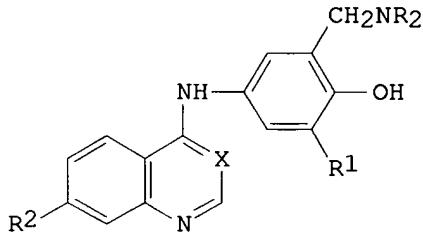
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and antiarrhythmic activity of)

RN 81080-33-3 HCPLUS

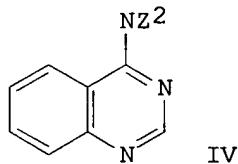
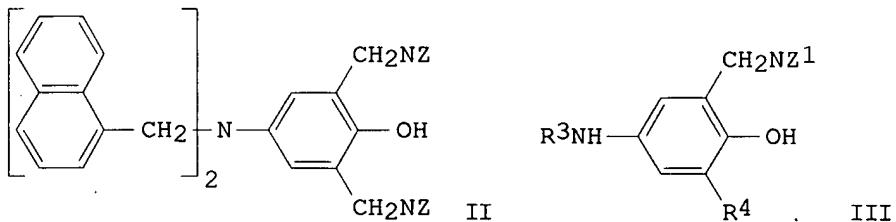
CN Phenol, 2-[(diethylamino)methyl]-4-[(6,7-dimethoxy-4-quinazolinyl)amino]-
 (9CI) (CA INDEX NAME)



L6 ANSWER 200 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:122727 HCPLUS
 DOCUMENT NUMBER: 96:122727
 TITLE: Studies on drugs for coronary diseases. II.
 Synthesis of compounds related to changrolin, a new antiarrhythmic agent
 AUTHOR(S): Sun, Cunji; Zhang, Xinyi; Yang, Xingzhong; Wang, Pingping; Shen, Jian; Shu, Yun; Ji, Ruyun; Kyi, Zuyoong
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. China
 SOURCE: Yaoxue Xuebao (1981), 16(8), 564-70
 DOCUMENT TYPE: CODEN: YHHPAL; ISSN: 0513-4870
 LANGUAGE: Chinese
 GI



I

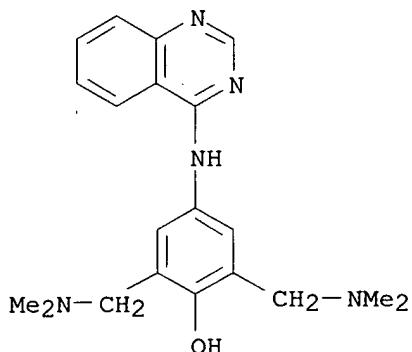


AB Changrolin (I; NR2 = 1-pyrrolidinyl, R1 = 1-pyrrolidinylmethyl, R2 = H, X = N) analogs, i.e., I [NR2 = NMe2, N(CH2CH2OH)2, morpholino, etc; R1 = H, CH2NR2; R2 = H; X = N], I (NR2 = NMe2, 1-pyrrolidinyl; R1 = H, CH2NR2; R2 = Cl; X = CH), II (NZ = NMe2, 1-pyrrolidinyl, 1-piperidinyl, morpholino), III (NZ1 = NMe2, 1-pyrrolidinyl, morpholino, etc.; R3 = Ac, Bz; R4 = H, CH2NZ1) and IV (NZ2 = NMe2, 1-pyrrolidinyl, morpholino, etc.) were prepared by known reactions. III (NZ1 = 1-pyrrolidinyl, R3 = Bz, R4 = CH2NZ1) was more effective than changrolin in protecting dogs from arterial fibrillation.

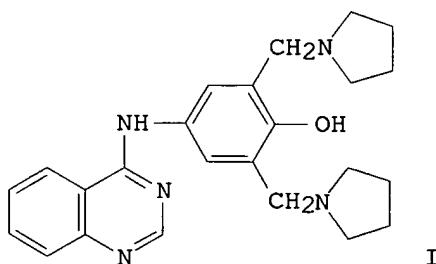
IT 81079-84-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and antiarrhythmic activity of)

RN 81079-84-7 HCAPLUS
 CN Phenol, 2,6-bis[(dimethylamino)methyl]-4-(4-quinazolinylamino)- (9CI) (CA
 INDEX NAME)



L6 ANSWER 201 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:79607 HCAPLUS
 DOCUMENT NUMBER: 96:79607
 TITLE: Electrophysiological effects of changrolin, a new antiarrhythmic drug, on isolated cardiac preparations
 AUTHOR(S): Xu, Y. Q.; Carmeliet, E.
 CORPORATE SOURCE: Lab. Physiol., Univ. Leuven, Louvain, Belg.
 SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1981), 253(2), 333-4
 CODEN: AIPTAK; ISSN: 0003-9780
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



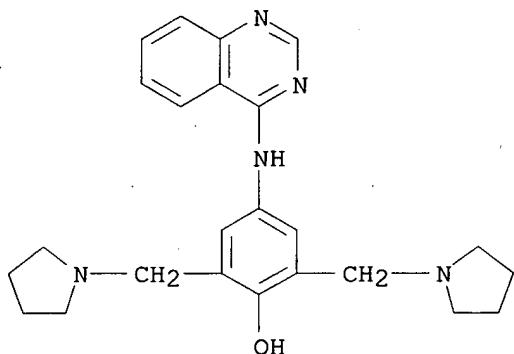
I

AB The electrophysiol. effects of changrolin (I) [72063-47-9] (1, 3, 10, and 20 mg/L) were studied in guinea pig auricular and ventricular muscle, and sheep ventricular muscle and Purkinje fibers. In prepns. stimulated at 60/min, I had no effect on maximum diastolic potential, except for a 5% depolarization in Purkinje fibers at 20 mg/L. The maximum rate of depolarization during upstroke (Vmax) and the amplitude of the action potential were decreased in a concentration-dependent manner. The depression of Vmax was strongly frequency-dependent but not potential-dependent. I had no effect on the Ca2+-mediated action potential. The effects of I were comparable to those of quinidine.

IT 72063-47-9

RL: BIOL (Biological study)
 (heart elec. activity response to)

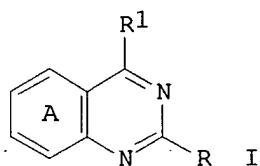
RN 72063-47-9 HCAPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA
 INDEX NAME)



L6 ANSWER 202 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1982:8146 HCAPLUS
 DOCUMENT NUMBER: 96:8146
 TITLE: Chromogenic quinazoline compounds and their use as color constituents in pressure-sensitive or heat-sensitive recording materials
 INVENTOR(S): Fletcher, Ian John
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 36 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------|------|----------------|-----------------|----------|
| EP 33716 | A1 | 19810812 | EP 1981-810019 | 19810126 |
| EP 33716 | B1 | 19830525 | | |
| R: AT, BE, CH, DE, FR, GB, IT | | | | |
| FI 8004067 | A | 19810801 | FI 1980-4067 | 19801230 |
| FI 70036 | B | 19860131 | | |
| FI 70036 | C | 19860912 | | |
| US 4480096 | A | 19841030 | US 1981-227294 | 19810122 |
| AT 3547 | T | 19830615 | AT 1981-810019 | 19810126 |
| CA 1162193 | A1 | 19840214 | CA 1981-369639 | 19810129 |
| BR 8100571 | A | 19810818 | BR 1981-571 | 19810130 |
| ES 498980 | A1 | 19820501 | ES 1981-498980 | 19810130 |
| JP 56120768 | A | 19810922 | JP 1981-12263 | 19810131 |
| JP 01056103 | B | 19891128 | | |
| US 4435003 | A | 19840306 | US 1982-421205 | 19820922 |
| PRIORITY APPLN. INFO.: | | CH 1980-780 | A 19800131 | |
| | | CH 1980-5411 | A 19800715 | |
| | | US 1981-227294 | A3 19810122 | |
| | | EP 1981-810019 | A 19810126 | |

OTHER SOURCE(S): MARPAT 96:8146
 GI



AB Chromogenic compds. of general structure I are prepared, where R represents an optionally substituted p-aminophenyl or carbazol-3-yl group, R1 represents H, alkoxy, aryloxy, amino, or thio ether derivative, and ring A may be substituted. I give sublimation- and lightfast yellow, orange, or red colors when in contact with acidic developers. Thus, reaction of 4-chloro-2-[4-(dimethylamino)phenyl]quinazoline [79916-53-3] with NaOMe in refluxing MeOH gave I (R = C₆H₄NMe₂-p, R1 = OMe) [79916-30-6], a yellow color former. Twenty other I were prepared

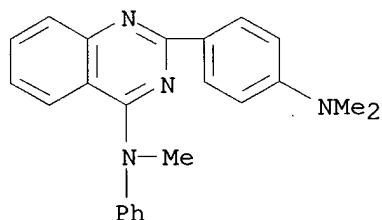
IT 79916-31-7P

RL: PREP (Preparation)

(manufacture of, as color former for heat- and pressure-sensitive recording materials)

RN 79916-31-7 HCPLUS

CN 4-Quinazolinamine, 2-[4-(dimethylamino)phenyl]-N-methyl-N-phenyl- (9CI)
(CA INDEX NAME)



L6 ANSWER 203 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:597122 HCPLUS

DOCUMENT NUMBER: 95:197122

TITLE: Physiological disposition of changrolin

AUTHOR(S): Zeng, Yan Lin; Yi, Qing Cheng; Gu, Hao Ming; Qu, Zhi Xiang; Xu, Guo Ying

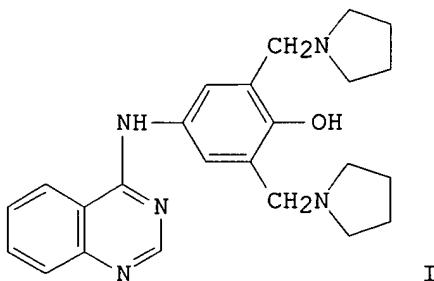
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci.,
Shanghai, 200031, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1981), 2(3), 177-81
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



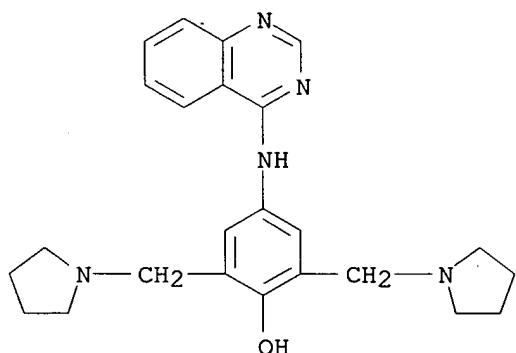
AB After administration of changrolin (I) [72063-47-9] (125 mg/kg, i.m.) to rats, 12 and 29.7% of I was excreted in the feces and urine, resp. Peak plasma I levels were 19-27 µg/mL at 15 min after drug administration. In rabbits, the urinary excretion of I was .apprx.22%. After 14C-labeled I was administered to mice, the radioactivity was highest in the liver and alimentary tract, moderate in the lungs and kidneys, and lowest in the heart, spleen, and brain. The bioavailabilities of I in rats were 78 and 64% after i.m. and intragastric administration, resp. Preliminary pharmacokinetic parameters for I using dogs, rabbits, and mice are presented.

IT 72063-47-9

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism and pharmacokinetics of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 204 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:515442 HCPLUS

DOCUMENT NUMBER: 95:115442

TITLE: Reactions of some 4(3H)quinazolinones

AUTHOR(S): Anwar, M.

CORPORATE SOURCE: Fac. Sci., Tanta Univ., Tanta, Egypt

SOURCE: Revue Roumaine de Chimie (1981), 26(4), 639-45

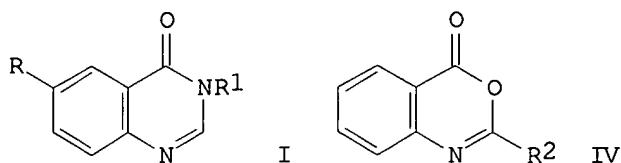
CODEN: RRCHAX; ISSN: 0035-3930

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 95:115442

GI



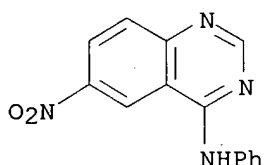
AB The reaction of I ($R = H, NO_2$; $R1 = H$) with halo compds. gave I [$R = H, R1 = Me$ (II), Ac (III); $R = NO_2, R1 = Me, Et, Ac, Bz, SO_2C_6H_4Me-4$]. III and IV ($R2 = Ph, CH:CHC_6H_4OMe-4, CH:CHC_6H_4Cl-2$) underwent aminolysis. II underwent fusion with aldehydes, ketones, benzil, and anilides. II condensed with maleic, succinic, and phthalic anhydrides. III underwent condensation with aldehydes.

IT 49675-75-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with quinazolinones)

RN 49675-75-4 HCPLUS

CN 4-Quinazolinamine, 6-nitro-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 205 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:443163 HCPLUS

DOCUMENT NUMBER: 95:43163

TITLE: 4-(N-Alkylanilino)quinazoline derivatives

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

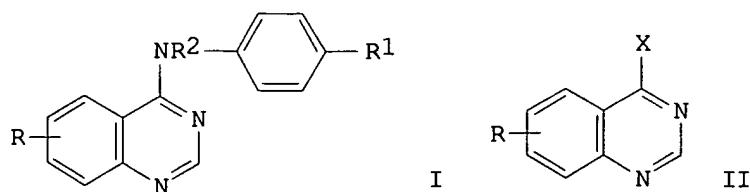
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|----------|----------|-----------------|------------|
| JP 56020577 | A | 19810226 | JP 1979-95815 | 19790727 |
| JP 62006715 | B | 19870213 | | |
| PRIORITY APPLN. INFO.: | | | JP 1979-95815 | A 19790727 |
| OTHER SOURCE(S): | CASREACT | 95:43163 | | |
| GI | | | | |



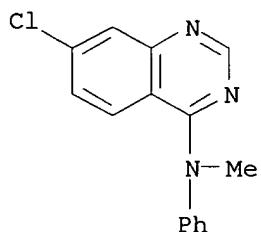
AB Fourteen title derivs. I (R = H, halo, CF₃, NO₂; R₁ = H, alkyl, alkoxy, halo; R₂ = alkyl) were prepared by heating II (X = halo) with 4-R₂NHC₆H₄R₁. Analgesic and antiinflammatory data of I were given in guinea pigs and rats, resp. Thus, heating 3 g II (R = 7-Cl, X = Cl) with 1.7 g PhNHMe in EtOH 10 min gave 46% I.HCl (R = 7-Cl, R₁ = H, R₂ = Me).

IT 74303-55-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic and antiinflammatory activities of)

RN 74303-55-2 HCPLUS

CN 4-Quinazolinamine, 7-chloro-N-methyl-N-phenyl-, monohydrochloride (9CI)
(CA INDEX NAME)



● HCl

L6 ANSWER 206 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:407199 HCPLUS

DOCUMENT NUMBER: 95:7199

TITLE: Studies in potential filaricides: Part XI. Synthesis of 2-(dialkylaminomethyl)-4-substituted aminophenols as amodiaquine analogs

AUTHOR(S): Agrawal, V. K.; Sharma, Satyavan; Iyer, R. N.; Chatterjee, R. K.; Sen, A. B.

CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1980), 19B(12), 1084-7

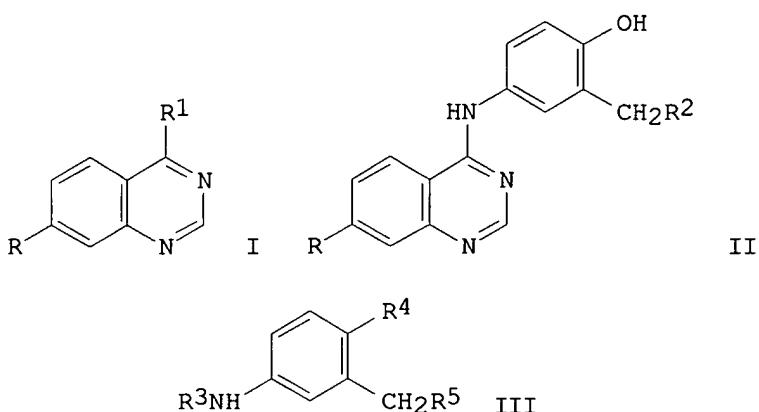
CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 95:7199

GI

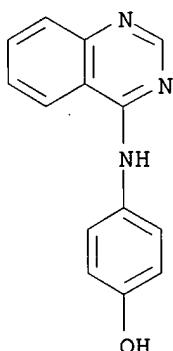


AB Condensing quinazolines I ($R = H, Cl$; $R' = Cl$) with 4- $\text{PhCH}_2\text{OC}_6\text{H}_4\text{NH}_2$, followed by hydrogenolysis gave I ($R' = 4-\text{HOCH}_2\text{C}_6\text{H}_4\text{NH}_2$), Mannich reaction of which gave II ($R_2 = \text{NET}_2$, 4-methylpiperazinyl, 4-hydroxy-4-phenylpiperidino). Mannich reaction of $\text{R}_3\text{NHC}_6\text{H}_4\text{R}_4-4$ ($R_3 = \text{Ac}, \text{NO}_2$; $R_4 = \text{OH}, \text{SH}$) gave III ($R_5 = \text{NET}_2$, pyrrolidinyl, 4-methylpiperazinyl, MeNCH_2Ph , 4-phenylpiperazinyl). III ($R_3 = \text{Ac}$, $R_4 = \text{OH}$, $R_5 = \text{NET}_2$) showed filaricidal activity at 30 mg/kg i.p. daily for 6 days in rats.

IT 34923-98-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and Mannich reaction of)

RN 34923-98-3 HCAPLUS

CN Phenol, 4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 207 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:400230 HCAPLUS
DOCUMENT NUMBER: 95:230
TITLE: Autocorrelation of molecular structures. Application to SAR studies
AUTHOR(S): Moreau, Gilles; Broto, Pierre
CORPORATE SOURCE: Dep. Phys., Roussel Uclaf, Romainville, 93230, Fr.
SOURCE: Nouveau Journal de Chimie (1980), 4(12), 757-64
CODEN: NJCHD4; ISSN: 0398-9836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new mol. descriptor, the autocorrelation of topol. structure, is used in a structure-activity relation to predict analgesic activity of 309

glafenine derivs. and isoindomethacine analogs. Using learning machine techniques the prediction of analgesic activity is shown to be in agreement with exptl. observed activity.

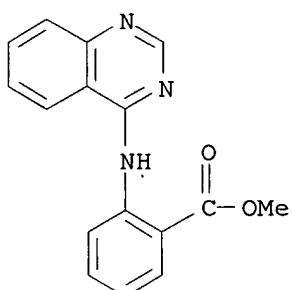
IT 49712-49-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(analgesic activity of, autocorrelation of topol. structure in relation to)

RN 49712-49-4 HCAPLUS

CN Benzoic acid, 2-(4-quinazolinylamino)-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 208 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:167780 HCAPLUS

DOCUMENT NUMBER: 94:167780

TITLE: Effects of antiarrhythmic drug changrolin on myocardial contractility in anesthetized dogs

AUTHOR(S): Shen, You-Tang; Wu, Pei-Ming; Wan, Fen-Ti; Chen, Wei-Zhou; Dong, Yue-Li

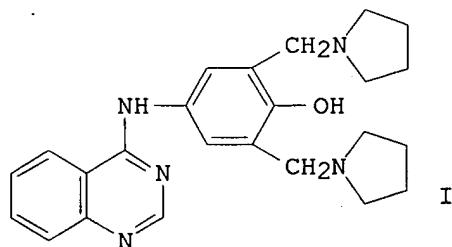
CORPORATE SOURCE: Shu Guang Hosp., Shanghai Traditional Chin. Med. Coll., Shanghai, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1981), 2(1), 23-6
CODEN: CYLPDN; ISSN: 0253-9756

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



AB Changes in ECG parameters demonstrated a pronounced antiarrhythmic effect of changrolin (I) [72063-47-9] (1 mg/kg/min, i.v.) in dogs. The development of these changes correlated linearly with the increase in plasma I level. The antiarrhythmic effect of I was reversible upon cessation of the infusion.

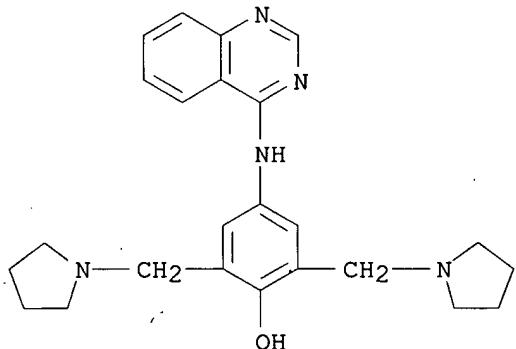
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 209 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:114415 HCAPLUS

DOCUMENT NUMBER: 94:114415

TITLE: Effects of infusion rate of Changrolin on drug concentration in blood and ECG

AUTHOR(S): Qu, Zhi-Xiang; Cao, Cui-Yu; Zhuang, Yi-Hua

CORPORATE SOURCE: Shanghai Inst. Materia Med., Acad. Sin., Shanghai, Peop. Rep. China

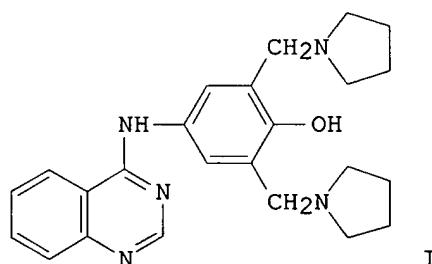
SOURCE: Yaoxue Xuebao (1980), 15(8), 449-55

CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI

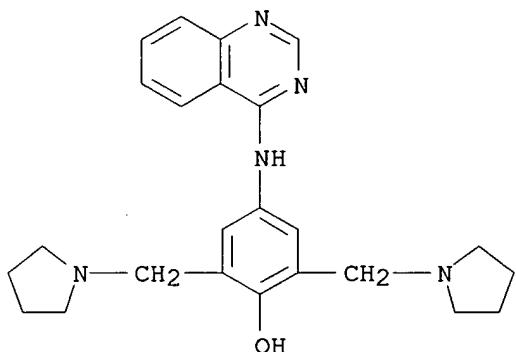


I

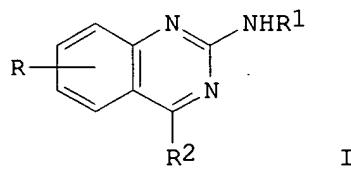
AB Infusion of Changrolin (I) [72063-47-9] at the rate of 0.13 mg/kg/min for 120 min to anesthetized dogs gave more uniform blood levels than did infusion at 5 mg/kg/min for 2 min or 1 mg/kg/min for 30 min. Further, less of a change in ECG was observed at the lowest dose rate. At the lowest dose rate, the heart rate increased slightly at the beginning and as the drug concentration rose above 5 mg/mL, the heart rate decreased gradually. The ECG showed a prolongation of the PR interval and widening of the QRS complex. Atrioventricular conduction was more sensitive to the drug than intraventricular conduction.

IT 72063-47-9

RL: BIOL (Biological study)
 (heart ECG response to, pharmacokinetics in relation to)
 RN 72063-47-9 HCPLUS
 CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA
 INDEX NAME)



L6 ANSWER 210 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1981:57955 HCPLUS
 DOCUMENT NUMBER: 94:57955
 TITLE: Synthesis and antimalarial effects of
 N2-aryl-N4-[(dialkylamino)alkyl]- and
 N4-aryl-N2-[(dialkylamino)alkyl]-2,4-
 quinazolininediamines
 AUTHOR(S): Elslager, Edward F.; Hess, Carolyn; Johnson, Judith;
 Ortwine, Daniel; Chu, Vera; Werbel, Leslie M.
 CORPORATE SOURCE: Pharm. Res. Div., Warner-Lambert/Parke Davis, Ann
 Arbor, MI, 48106, USA
 SOURCE: Journal of Medicinal Chemistry (1981), 24(2), 127-40
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 94:57955
 GI

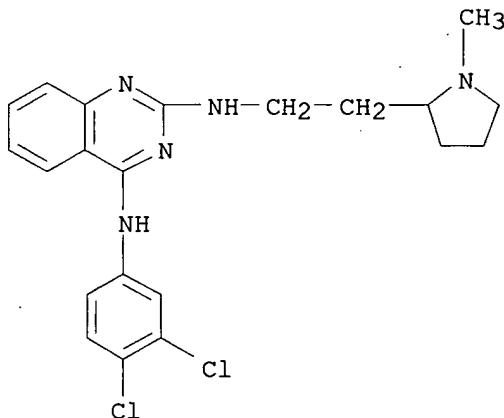


AB The title compds. I ($R = H, Cl, NH_2, NO_2$, etc.; $R1 =$ substituted Ph, heterocyclic, or dialkylaminoalkyl; $R2 =$ dialkylaminoalkyl, substituted heterocyclic, or substituted Ph) were prepared by stepwise reactions from either 2,4-dichloroquinazoline [607-68-1] or 2-chloro-4-quinazolinol [607-69-2], and tested in mice for antimalarial activity.
 N2-(3,4-Dichlorophenyl)-N4-[2-(1-methyl-2-pyrrolidinyl)ethyl]-2,4-
 quinazolininediamine-2HCl [76004-48-3] was among the more active compds.
 Structure-activity relations are discussed.

IT 76005-10-2P

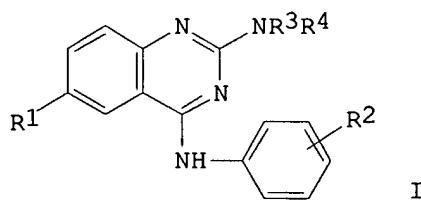
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and antimalarial activity of)
 RN 76005-10-2 HCAPLUS
 CN 2,4-Quinazolinediamine, N4-(3,4-dichlorophenyl)-N2-[2-(1-methyl-2-pyrrolidinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

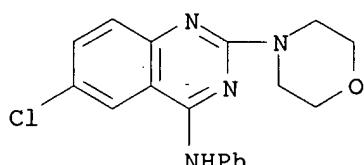
L6 ANSWER 211 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:604577 HCAPLUS
 DOCUMENT NUMBER: 93:204577
 TITLE: Synthesis of substituted 4-anilinoquinazolines
 AUTHOR(S): Stankovsky, Stefan; Martvon, Augustin
 CORPORATE SOURCE: Dep. Org. Chem., Slovak Inst. Technol., Bratislava,
 880 37, Czech.
 SOURCE: Collection of Czechoslovak Chemical Communications
 (1980), 45(4), 1079-85
 CODEN: CCCCAK; ISSN: 0366-547X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 93:204577
 GI



AB Thirteen 4-anilinoquinazolines I [R1 = H, Cl, Br, NO2; R2 = 4-NO2, 2-NO2, 4-Br; R3 = R4 = Me; R3 + R4 = (CH2)5, (CH2CH2)2O] were prepared in 20-65% yields by refluxing the equimol. amts. of amidinoyl isothiocyanates 4-R1C6H4N:C(NR3R4)NCS (II) and isothiocyanate R2C6H4NCS in DMF. The corresponding quinazoline-4(3H)thiones were the main byproducts. The 2 + 2 cycloaddn., CS2 elimination, and cyclization of unstable amidinoyl

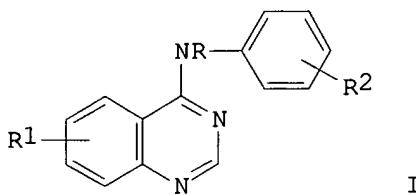
carbodiimine was suggested as the mechanism. I [R1 = NO₂, R2 = 4-NO₂, R3 + R4 = (CH₂)₅, or (CH₂CH₂)O₂] were also prepared in 30 and 25%, yield resp. by refluxing II [R1 = NO₂, R3 + R4 = (CH₂)₅, or (CH₂CH₂)O₂] in MeCN.

IT 60973-41-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 60973-41-3 HCAPLUS
 CN 4-Quinazolinamine, 6-chloro-2-(4-morpholinyl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 212 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:471802 HCAPLUS
 DOCUMENT NUMBER: 93:71802
 TITLE: 4-Anilinoquinazoline derivatives
 INVENTOR(S): Kobayashi, Shinsaku; Kamoshita, Katsuo; Nagai, Shigeki; Honda, Takeo; Oda, Kiroku; Fujii, Katsutoshi; Kobayashi, Takashi; Kojima, Mikio
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan; Ube Industries, Ltd.
 SOURCE: Ger. Offen., 36 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------------------------------------|----------|-----------------|-------------|
| DE 2936705 | A1 | 19800320 | DE 1979-2936705 | 19790911 |
| JP 55038325 | A | 19800317 | JP 1978-111484 | 19780911 |
| JP 62006546 | B | 19870212 | | |
| DK 7903770 | A | 19800312 | DK 1979-3770 | 19790910 |
| SE 7907493 | A | 19800312 | SE 1979-7493 | 19790910 |
| SE 446337 | B | 19860901 | | |
| SE 446337 | C | 19861211 | | |
| CA 1151168 | A1 | 19830802 | CA 1979-335246 | 19790910 |
| CH 642361 | A5 | 19840413 | CH 1979-8166 | 19790910 |
| BE 878723 | A1 | 19800311 | BE 1979-197102 | 19790911 |
| NL 7906761 | A | 19800313 | NL 1979-6761 | 19790911 |
| FR 2435248 | A1 | 19800404 | FR 1979-22639 | 19790911 |
| FR 2435248 | B1 | 19830218 | | |
| GB 2033894 | A | 19800529 | GB 1979-31441 | 19790911 |
| GB 2033894 | B | 19830216 | | |
| ES 484097 | A1 | 19801101 | ES 1979-484097 | 19790911 |
| US 4322420 | A | 19820330 | US 1979-74343 | 19790911 |
| US 4464375 | A | 19840807 | US 1981-289379 | 19810803 |
| PRIORITY APPLN. INFO.: | | | JP 1978-111484 | A 19780911 |
| | | | US 1979-74343 | A3 19790911 |
| OTHER SOURCE(S): | CASREACT 93:71802; MARPAT 93:71802 | | | |
| GI | | | | |



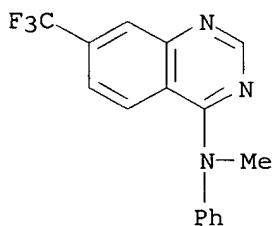
AB The title compds. (I; R = H, alkyl; R1 = H, halogen, CF₃, NO₂; R2 = H, alkyl, alkoxy, halogens) and their salts were prepared for use as analgesics and antiinflammatory agents, with activity comparable to or exceeding that of aspirin. Thus, 4,5-dichloroquinazoline was heated with PhNH₂ in EtOH to give 46% I.HCl (R = R2 = H, R1 = 5-Cl).

IT 74303-60-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oxidation and analgesic activity of)

RN 74303-60-9 HCPLUS

CN 4-Quinazolinamine, N-methyl-N-phenyl-7-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 213 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:400795 HCPLUS

DOCUMENT NUMBER: 93:795

TITLE: Cardiovascular effect of a new antiarrhythmic drug-changrolin

AUTHOR(S): Chen, Wei-Zhou; Dong, Yue-Li; Ding, Guang-Sheng

CORPORATE SOURCE: Shanghai Inst. Mat. Med., Acad. Sin., Shanghai, Peop. Rep. China

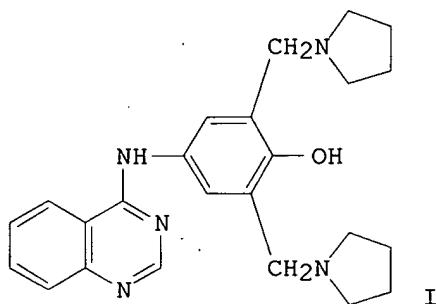
SOURCE: Yaoxue Xuebao (1979), 14(12), 710-14

CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI

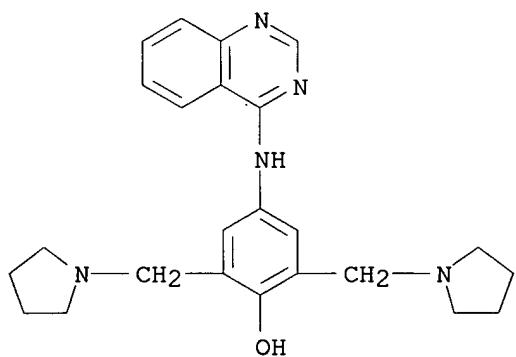


AB Changrolin (I) [72063-47-9] (30 mg/kg, i.v.) displayed cardiovascular effects similar to that of quinidine in dogs. It decreased blood pressure, left ventricular systolic pressure, and cardiac output, but not total peripheral resistance. EKG changes included lengthening of the QRS, P-R, and Q-Tc intervals. I had a cardiac-vagal blocking effect but no adrenergic blocking effect. I inhibited ouabain-induced ventricular tachycardia; this effect was obtained at plasma I levels of 0.61 µg/mL.

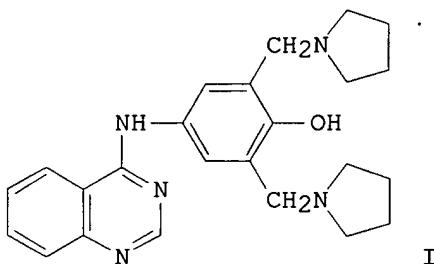
IT 72063-47-9
 RL: PRP (Properties)
 (cardiovascular effects of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 214 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:174588 HCAPLUS
 DOCUMENT NUMBER: 92:174588
 TITLE: Effects of changrolin on coronary circulation and post-infarction ventricular arrhythmia in dogs
 AUTHOR(S): Chen, Wei-Zhou; Dong, Yue-Li; Wahg, Chang-Gen; Ting, Kuang-Sheng; Yang, Hsueh-Yi
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. China
 SOURCE: Shengli Xuebao (1979), 31(4), 382-6
 CODEN: SLHPAH; ISSN: 0371-0874
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



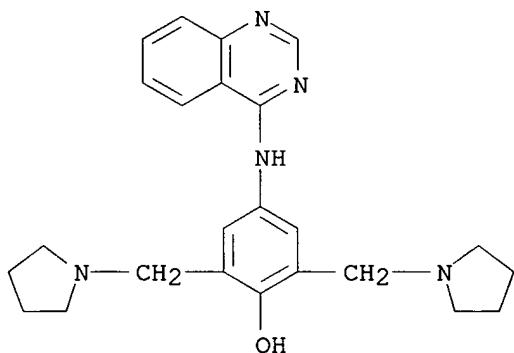
AB In 7 anesthetized open-chest dogs, an i.v. injection of changrolin (I) [72063-47-9] (7 mg/kg) lowered the blood pressure and the work load of the left ventricle. The decrease in the coronary and aortic blood flow was not significant, while the coronary vascular resistance tended to decline. During the period of lowering of the work done by the left ventricle, the myocardial utilization of O₂, lactic acid, and pyruvic acid were not affected. Two-stage left anterior coronary ligation was performed in 6 anesthetized dogs. After 24 h, severe ventricular arrhythmias were recorded in the conscious state. An i.v. bolus of 5 mg I/kg produced a remarkable antiarrhythmic effect lasting about half an h. The P-R interval, QRS complex and A-T interval of sinus rhythm were not much altered.

IT 72063-47-9

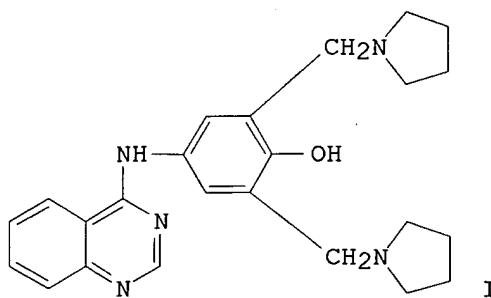
RL: BIOL (Biological study)
(coronary circulation and heart arrhythmia response to)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 215 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:174188 HCAPLUS
 DOCUMENT NUMBER: 92:174188
 TITLE: Intracellular distribution of Changrolin
 AUTHOR(S): Tu, Zeng-Hong; Chen, En-Hong; Wu, Wei-Wei; Yang, Hui-Hua
 CORPORATE SOURCE: Dep. Pharmacol., Shanghai Inst. Mater. Med., Shanghai, Peop. Rep. China
 SOURCE: Yaoxue Xuebao (1979), 14(10), 594-7
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



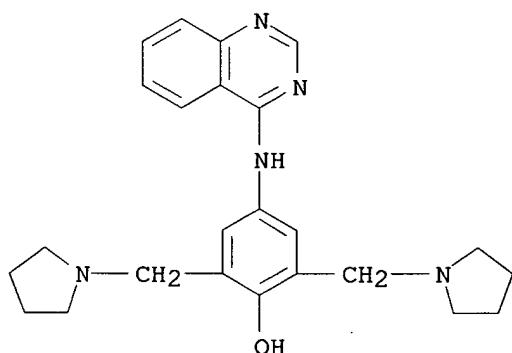
AB After administration of the antiarrhythmic drug changrolin (I) [72063-47-9] to rabbits the myocardium was separated into nuclear, mitochondrial, and supernatant fractions. Most of I was found in the supernatant fraction, part of which being associated with cytoplasmic proteins. Some of the I dose was present in the nuclear fraction as well.

IT 72063-47-9

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of heart myocardium)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 216 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:121950 HCAPLUS

DOCUMENT NUMBER: 92:121950

TITLE: Studies on a new antiarrhythmic drug changrolin
(4-{3',5'-bis[(N-pyrrolidinyl)methyl]-4'-hydroxyanilino}quinazoline)

AUTHOR(S): Li, Liang-Quan; Qu, Ahi-Xiang; Wang, Zhi-Min; Zeng, Yan-Lin; Ding, Guang-Sheng; Hu, Guo-Jun; Yang, Xue-Yi

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai,
Peop. Rep. China

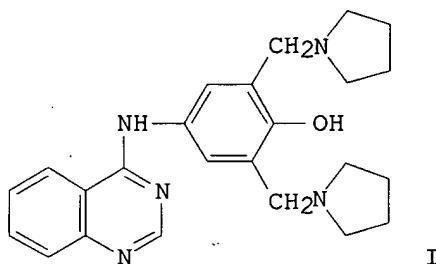
SOURCE: Scientia Sinica (English Edition) (1979), 22(10),
1220-8

CODEN: SSINAV; ISSN: 0582-236X

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



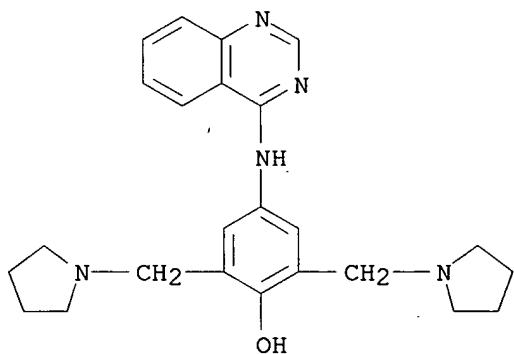
AB Changrolin (I) [72063-47-9] was prepared by cyclization of o-aminobenzoic acid [118-92-3] to the appropriate quinazolinone followed by chlorination to the 4-chloroquinazoline [5190-68-1] which after reaction with p-aminophenol [123-30-8] gave 4-(4-hydroxyanilino)quinazoline [34923-98-3] which in turn reacted with formaldehyde and pyrrolidine [123-75-1]. The antiarrhythmic activity of I as the HCl was demonstrated in aconitine-induced arrhythmia in rats. I was also effective in ouabain-induced arrhythmia in dogs, and on elec. fibrillation threshold in rabbits. I was best absorbed by i.m. route. In clin. trials I was most effective in treating paroxysmal ventricular tachycardia and ventricular premature beats.

IT 72063-47-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antiarrhythmic activity and pharmacokinetics of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 217 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:76445 HCPLUS

DOCUMENT NUMBER: 92:76445

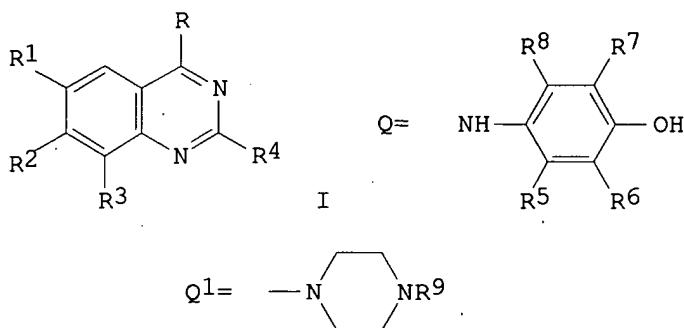
TITLE: Synthesis of shangrolin analogs as antimalarials

AUTHOR(S): Li, Ying; Li, Liang-Quan; Chen, Yi-Xin; Wang, De-Sheng; Gai, Yuan-Zhu; Yu, Pei-Lin; Zheng, Ya-Ping
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. ChinaSOURCE: Yaoxue Xuebao (1979), 14(2), 108-15
CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



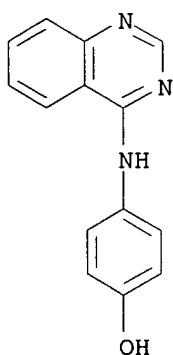
AB Shangrolin analogs I ($R = Q, Q^1; R1 = H, Cl, MeO; R2 = H, MeO; R1R2 = OCH_2O; R4 = R5 = R8 = H, Me; R6 = H, 1\text{-pyrrolidinylmethyl (Q2)}; R7 = H, Q2, 1\text{-adamantylaminomethyl; R9 = H, 2-, 3-C}_1\text{C}_6\text{H}_4$) were prepared by amination of I ($R = Cl$) and Mannich reaction of I ($R = Q; R6 = R7 = H$). Pteridine analog of shangrolin and 1,3-bis[4-(6,8-dichloroquinazolin-4-yl)piperazin-1-yl]propane were also prepared I ($R = Q; R1 = R2 = R3 = R5 = R8 = H; R4 = Me, R6 = R7 = Q2$ and $R1R2 = OCH_2O; R3 = R4 = R5 = R7 = R8 = H, R6 = Q2$) were more active than shangrolin against *P. berghei* in mice.

IT 34923-98-3

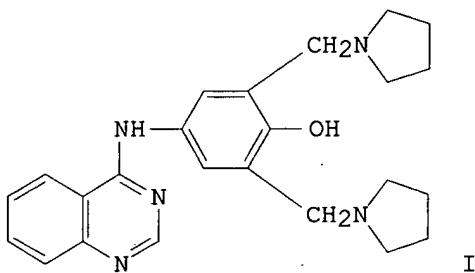
RL: RCT (Reactant); RACT (Reactant or reagent)
(Mannich reaction of)

RN 34923-98-3 HCPLUS

CN Phenol, 4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 218 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:51919 HCPLUS
 DOCUMENT NUMBER: 92:51919
 TITLE: Antiarrhythmic effect of 4-[3',5'-bis[(N-pyrrolidinyl)methyl]-4'-hydroxyanilino] quinazoline (changrolin) on aconitine-induced arrhythmia in rats
 AUTHOR(S): Wang, Zhi-Min; Zhang, Yue-Fang; Ting, Kuang Sheng
 CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. China
 SOURCE: Yaoxue Xuebao (1979), 14(7), 408-11
 CODEN: YHHPAL; ISSN: 0513-4870
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 GI



AB I.v. injections of changrolin (I) [72063-47-9] followed by or concomitant with injections of aconitine inhibited the onset of aconitine-induced arrhythmia. If I was given after the onset of arrhythmia, its antiarrhythmic effect was weaker. Neither bilateral vasotomy nor i.v. injections of hexamethonium modified the antiarrhythmic effect of I. The dose thresholds for ventricular premature beats, ventricular tachycardia and ventricular fibrillation during i.v. infusion of aconitine at constant rate were all raised by a pretreatment with I, and further augmented by a previous reserpination. Administration of I into the lateral cerebral ventricle also retarded the onset of arrhythmia induced by a subsequent intracerebral introduction of aconitine. On the sciatic nerves of rats I showed a very mild local anesthetic action, which was different from that of lidocaine.

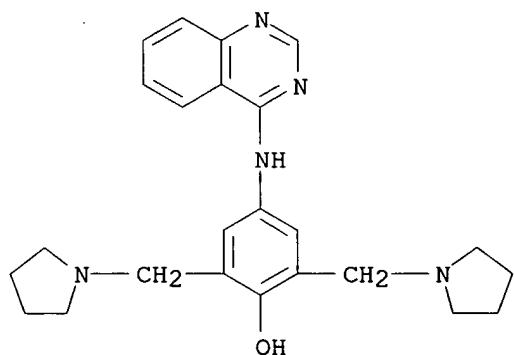
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of)

RN 72063-47-9 HCPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 219 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:51740 HCPLUS

DOCUMENT NUMBER: 92:51740

TITLE: Effect of a new potent antiarrhythmic drug Changrolin on the electrical activity of myocardial cells

AUTHOR(S): Fan, Shin-Fang; Hsu, Sen-Gen; Zhou, Nian-Hui

CORPORATE SOURCE: Shanghai Inst. Physiol., Acad. Sin., Shanghai, Peop.

Rep. China

SOURCE: Shengli Xuebao (1979), 31(2), 175-84

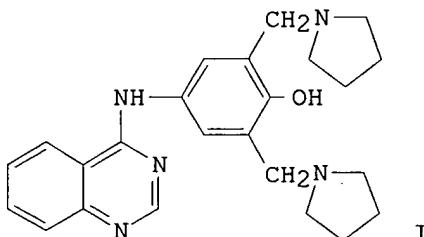
DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

GI



AB Changrolin (I) [72063-47-9] ($24 \mu\text{g/mL}$) decreased the amplitude and the maximum depolarization rate of phase 0 of the action potential of elec.-stimulated isolated guinea pig ventricular system endocardial cells. I increased the rate of depolarization of phase 2 and decreased its duration. The effective refractory period was increased. I decreased the effects of ouabain and aconitine on this preparation

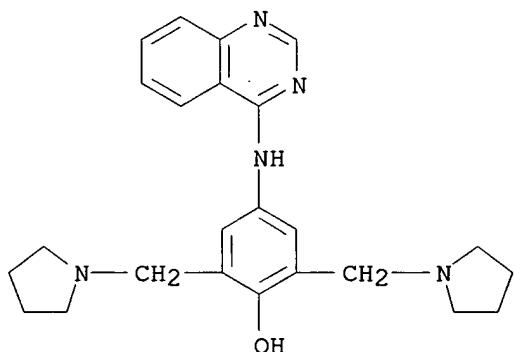
IT 72063-47-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarrhythmic activity of)

RN 72063-47-9 HCAPLUS

CN Phenol, 2,6-bis(1-pyrrolidinylmethyl)-4-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 220 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:557681 HCAPLUS

DOCUMENT NUMBER: 91:157681

TITLE: Heterocyclic compounds. XII. Quinazoline derivatives as potential antifertility agents

AUTHOR(S): Manhas, M. S.; Hoffman, W. A., III; Bose, A. K.

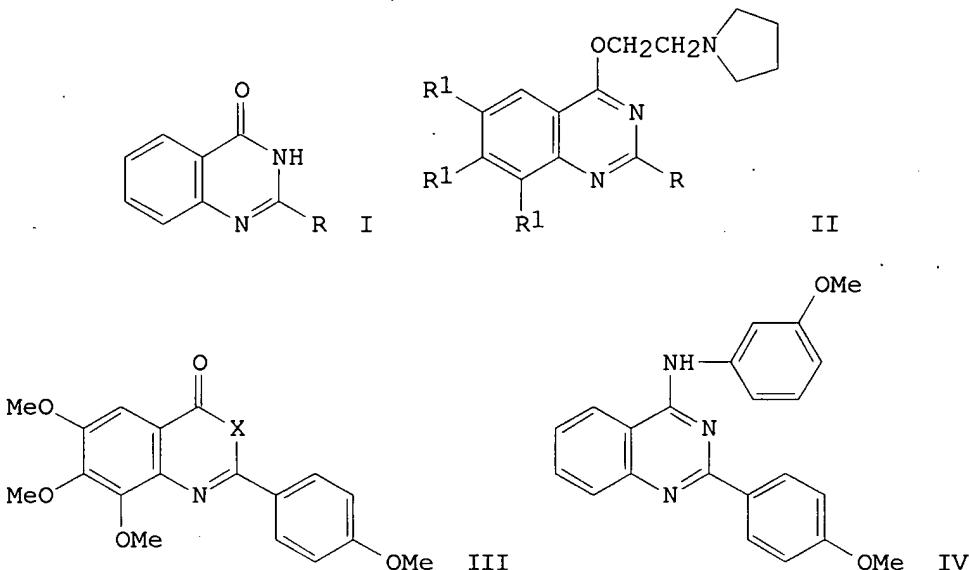
CORPORATE SOURCE: Dep. Chem. Eng., Stevens Inst. Technol., Hoboken, NJ, 07030, USA

SOURCE: Journal of Heterocyclic Chemistry (1979), 16(4), 711-15

DOCUMENT TYPE: CODEN: JHTCAD; ISSN: 0022-152X
Journal

LANGUAGE:
OTHER SOURCE(S):
GI

English
CASREACT 91:157681



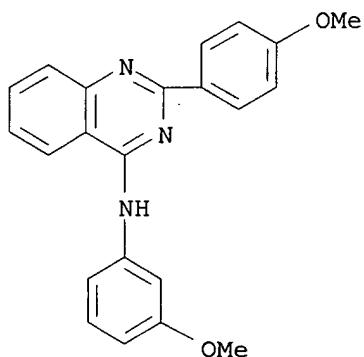
AB Acylation of 2-H₂NC₆H₄CONH₂ by RCOCl [R = 4-MeOC₆H₄, 4-MeOC₆H₄CH:CPh, α -benzylidene-3,4-dimethoxybenzyl, 3,4-methylenedioxyphenyl] gave 2-(RCONH)C₆H₄CONH₂, which cyclized in refluxing Ph₂O to give the corresponding quinazolinones I. Chlorination of I by POCl₃ followed by substitution reaction with 2-pyrrolidinoethanol Na salt gave ethoxyquinazolines II (R as defined above; R₁ = H). Hydrogenation of Me 3,4,5-trimethoxy-2-nitrobenzoate over Pt/C followed by acylation with 4-MeOC₆H₄COCl gave Me 2-(p-methoxybenzamido)-3,4,5-trimethoxybenzoate, which underwent cyclocondensation in refluxing C₆H₆ containing NaOMe to give the benzoxazinone III (X = O). Treatment of III (X = O) with NH₃ in MeOH under pressure gave III (X = NH), which underwent chlorination and substitution reaction with pyrrolidinoethanol Na salt to give II (R = 4-MeOC₆H₄; R₁ = MeO). Reaction of I (R = 4-MeOC₆H₄) with P₂S₅ gave the corresponding quinazolinethione, which underwent S-methylation with Me iodide and then substitution reaction with 3-MeOC₆H₄NH₂ to give the anilinoquinazoline IV. II (R = 4-MeOC₆H₄, α -benzylidene-3,4,5-trimethoxybenzyl, 3,4-methylenedioxyphenyl; R₁ = H) and IV possessed low level postcoital contraceptive activity in rats.

IT 71622-66-7P

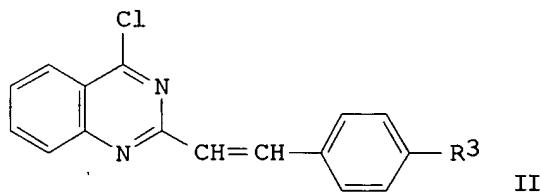
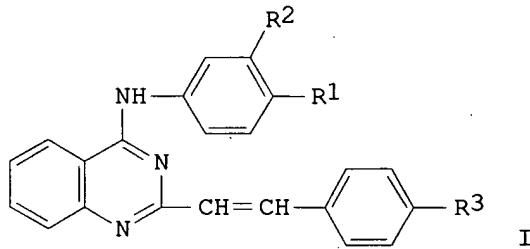
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 71622-66-7 HCAPLUS

CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 221 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1979:54902 HCAPLUS
 DOCUMENT NUMBER: 90:54902
 TITLE: Synthesis of some 2-styrylquinazoline derivatives structurally related to certain chemotherapeutic agents
 AUTHOR(S): Botros, S.; Shaban, M.
 CORPORATE SOURCE: Fac. Pharm., Cairo Univ., Cairo, Egypt
 SOURCE: Pharmazie (1978), 33(10), 646-7
 CODEN: PHARAT; ISSN: 0031-7144
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 90:54902
 GI



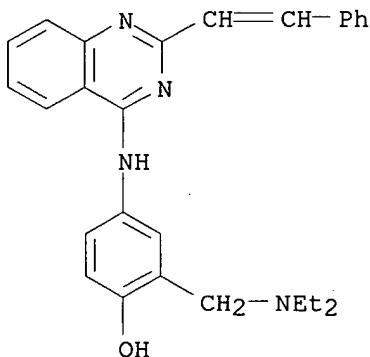
AB Aminostyrylquinazolines I ($R_1 = OH, OMe, OEt, Br, SO_2NH_2$; $R_2 = CH_2NET_2$, piperidinomethyl, H,; $R_3 = H, MeO$) were prepared in 86-95% yield by condensation of the chlorostyrylquinazolines (II) with amines. II were prepared in 64-7.8% yield by treatment of styrylquinazolones with $POCl_3$ and excess $PhNMe_2$.

IT 69018-97-9P

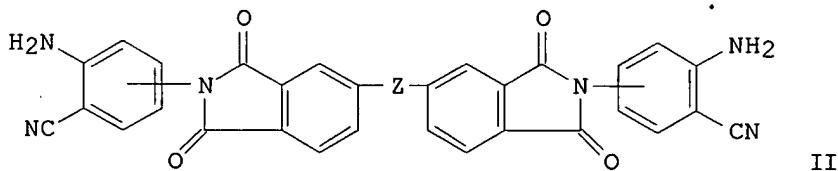
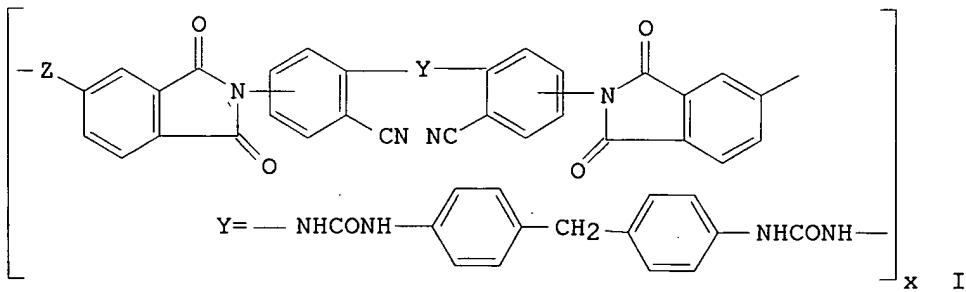
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 69018-97-9 HCAPLUS

CN Phenol, 2-[(diethylamino)methyl]-4-[[2-(2-phenylethenyl)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 222 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1978:529963 HCAPLUS
 DOCUMENT NUMBER: 89:129963
 TITLE: Synthesis and isomerization cyclization of poly(cyanoureas) containing imide units
 AUTHOR(S): Barashkov, N. N.; Evstaf'ev, V. P.; Telesov, E. N.; Pravednikov, A. N.
 CORPORATE SOURCE: Nauchno-Issled. Fiz.-Khim. Inst. im. Karpova, Moscow, USSR
 SOURCE: Vysokomolekulyarnye Soedineniya, Seriya A (1978), 20(7), 1586-92
 CODEN: VYSAAF; ISSN: 0507-5475
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI



AB Imide-containing poly(cyanoureas) (I, Z = O, CO) were prepared by polycondensation of N,N'-bis(o-aminocyanophenyl) diimides (II) with 4,4'-diphenylmethane diisocyanate at 60-70° in N-methylpyrrolidone in the presence of Ba3N catalyst. On heating I to 300° for 1 h, cyclization occurred with complete disappearance of the IR absorption for

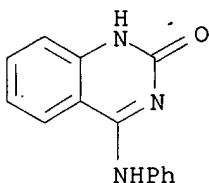
CN groups. A 2-stage cyclization is proposed, involving initial formation of an iminoquinazolinone structure which isomerizes to an aminoquinazolinone structure. The final polymer probably contains both structures. The noncyclized I had glass transition temps. 330-55° and exhibited initial weight loss at 395-440°. Rate consts. and activation energies are given for various stages of the cyclization-isomerization. The structure of the polymers was verified by synthesis of model compds. from anthranilonitrile [1885-29-6] and PhNCO [103-71-9].

IT 67461-77-2P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation and IR spectra of, as model compds. for poly(cyanourea) cyclization)

RN 67461-77-2 HCAPLUS

CN 2(1H)-Quinazolinone, 4-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 223 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:509338 HCAPLUS

DOCUMENT NUMBER: 89:109338

TITLE: Some reactions with 2-ethyl-4-quinazolone and 2-ethyl-4H-3,1-benzoxazone

AUTHOR(S): Selim, M.; Sammour, A.; Abdalla, M.; Elkasaby, M.

CORPORATE SOURCE: Fac. Sci., Ain Shams Univ., Cairo, Egypt

SOURCE: Pakistan Journal of Scientific Research (1975), 27(1-4), 67-72

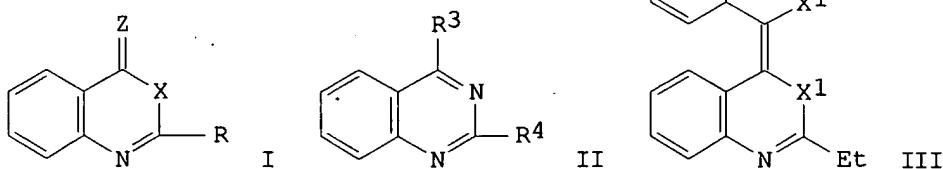
CODEN: PJSRAV; ISSN: 0552-9050

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 89:109338

GI



AB Quinazolone I ($R = Et$, $X = NH$, $Z = O$) reacted with HCHO and amines to give 75-80% Mannich bases I [$R = Et$, $Z = O$, $X = NCH_2R_1$ ($R_1 = morpholino$, piperidino, $PhNMe$)]. I ($R = Et$, $X = NH$, $Z = O$) and diazonium chlorides gave 60-74% a mixture of I [$R = CHMeN:NC_6H_4R_2$ ($R_2 = H$, 3-, 4-Me, 2- NO_2 , 3-,

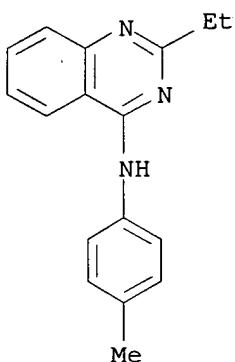
4-Cl, 2-MeO), X = NH, Z = O] and the tautomeric II (R3 = OH, R4 = CMe:NHC6H4R2). PC15-POC13 and I (R = Et, X = NH, Z = O) gave 80% II (R3 = Cl, R4 = Et) which reacted with amines to give 78-80% II [R3 = NHR5 (R5 = Bu, C6H4Me-4)]. I (R = Et, X = NH, O, Z = O) treated with P2S5 gave 55% I (R = Et, X = NH, Z = S) and its tautomer II (R3 = SH, R4 = Et) or 53% I (R = Et, X = Z = S), which condensed with cinnamaldehyde to give 64-5% the corresponding I (R = CMe:CHCH:CHPh) or II (R4 = CMe:CHCH:CHPh), or with Cu bronze to give 51-3% III (X1 = S, NH).

IT 67130-26-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 67130-26-1 HCPLUS

CN 4-Quinazolinamine, 2-ethyl-N-(4-methylphenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 224 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:507306 HCPLUS

DOCUMENT NUMBER: 89:107306

TITLE: Isomerization cyclization of N-phenyl-N'-(o-cyanophenyl)urea

AUTHOR(S): Barashkov, N. N.; Zimina, L. A.; Teleshov, E. N.; Pravednikov, A. N.

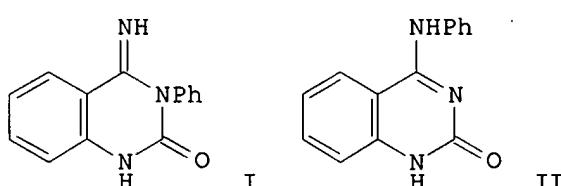
CORPORATE SOURCE: Fiz. Khim. Inst. im. Karpova, Moscow, USSR

SOURCE: Doklady Akademii Nauk SSSR (1978), 240(4), 847-50
[Chem.]

DOCUMENT TYPE: CODEN: DANKAS; ISSN: 0002-3264

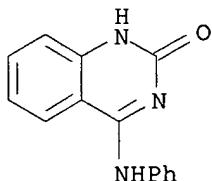
LANGUAGE: Journal

GI Russian

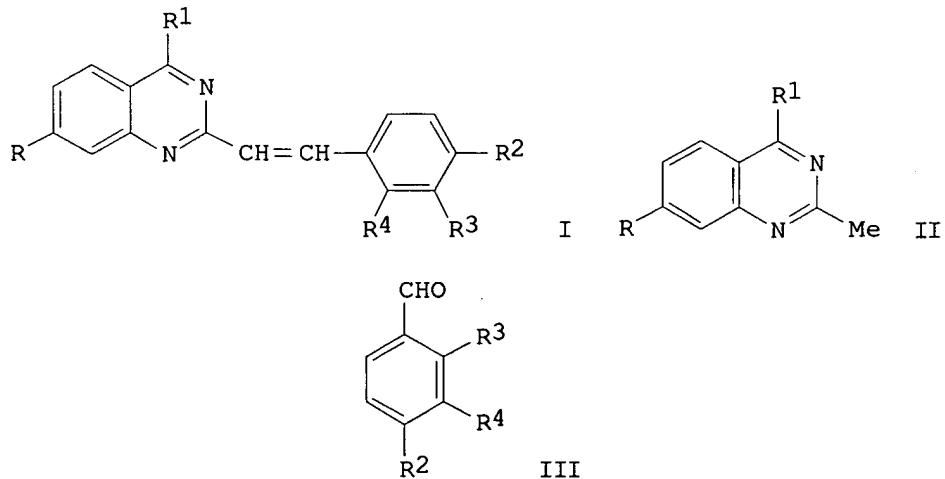


AB The kinetics of cyclization of 2-NCC6H4NHCONHPh to I (which could rearrange to give II) were determined in several solvents at 74°. The cyclization involved base-catalyzed addition of the N of the NHPh group to the C of the cyano group, followed by addition of H⁺ from BH⁺ to the C:N- group of the cyclic ion formed.

IT 67461-77-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 67461-77-2 HCAPLUS
 CN 2(1H)-Quinazolinone, 4-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 225 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1978:22828 HCAPLUS
 DOCUMENT NUMBER: 88:22828
 TITLE: Synthesis and study of the antiinflammatory effect of
 4-amino-2-styrylquinazolines
 AUTHOR(S): Zhikhareva, G. P.; Berlyand, E. A.; Liberman, S. S.;
 Yakhontov, L. N.
 CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst. im.
 Ordzhonikidze, Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1977), 11(10),
 58-62
 CODEN: KHFZAN; ISSN: 0023-1134
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 OTHER SOURCE(S): CASREACT 88:22828
 GI



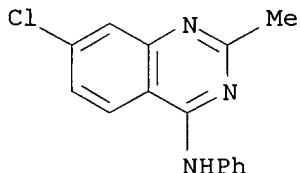
AB The title compds. I [R = H, Cl; R1 = NCHMe(CH2)3NET2, NET2, NHPh, piperidino; R2 = OMe, NO2, Cl, H, OH; R3 = H, Cl, R4 = H, OMe] useful as inflammation inhibitors, were obtained in 28-66% yields by condensation of quinazolines II with aldehydes III.

IT 57942-23-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzaldehyde derivs.)

RN 57942-23-1 HCAPLUS

CN 4-Quinazolinamine, 7-chloro-2-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 226 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1977:584175 HCAPLUS

DOCUMENT NUMBER: 87:184175

TITLE: Acyl carbodiimides, II. Preparation, stability, and addition reactions of imidoylecarbodiimides

AUTHOR(S): Goerdeler, Joachim; Lohmann, Helmut

CORPORATE SOURCE: Inst. Org. Chem. Biochem., Univ. Bonn, Bonn, Fed. Rep. Ger.

SOURCE: Chemische Berichte (1977), 110(9), 2996-3009

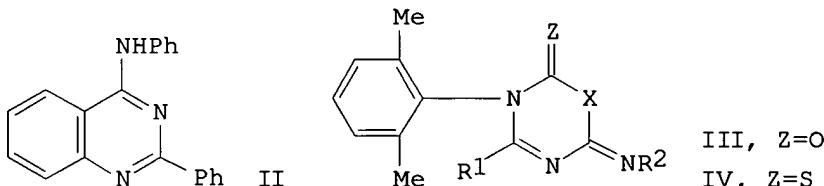
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 87:184175

GI



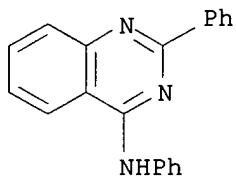
AB RN:CR1NHCSNHR2 (R = Me, CHMe₂, Ph, 2,6-Me₂C₆H₃, 1-naphthyl; R₁ = Ph, 4-ClC₆H₄, 4-O₂NC₆H₄; R₂ = cyclohexyl, Ph, CMe₃, 2,6-Me₂C₆H₃, Me), prepared from RN:CR1Cl, NaSCN, and R₂NH₂ in Me₂CO at 0°, reacted with cyanuric chloride in CH₂C₁₂, containing NET₃ with H₂S elimination to give RN:CR1N:C:NR2 (I), some of which could be isolated. The stability of I was substituent dependent. Thus, alkyl groups at R were especially destabilizing and the 2,6-Me₂C₆H₃ group at R was strongly stabilizing. I (R = R₁ = Ph) tended to isomerize to the quinazoline derivative II. I added nucleophilic HX compds. (H₂O, EtOH, PhOH, EtSH, PhSH, PhNH₂, cyclohexylamine) to give RN:CR1NHCONHR2 and 2,6-Me₂C₆H₃N:C(C₆H₄NO₂-4)NHCX:NR2 and formed cycloaddn. compds. III [R₁ = 4-ClC₆H₄, 4-O₂NC₆H₄, R₂ = cyclohexyl, Me; X = CPh₂, NR₃ (R₃ = Ph)] and IV [R₁ = 4-O₂NC₆H₄, R₂ = cyclohexyl; X = NR₃ (R₃ = Bz, 4-O₂NC₆H₄CO, EtO₂C] with Ph₂C:C:O, PhOCN, BzNCO, 4-O₂NC₆H₄NCO, and EtO₂CNCS.

IT 40288-70-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 40288-70-8 HCAPLUS

CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 227 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1977:43733 HCAPLUS

DOCUMENT NUMBER: 86:43733

TITLE: 4-Aminoquinazolines

INVENTOR(S): Foster, Charles H.

PATENT ASSIGNEE(S): Eastman Kodak Co., USA

SOURCE: U.S., 4 pp.

CODEN: USXXAM

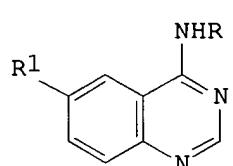
DOCUMENT TYPE: Patent

LANGUAGE: English

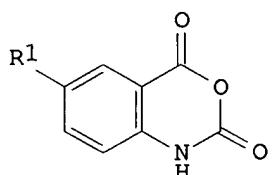
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------|------|----------|-----------------|------------|
| US 3985749 | A | 19761012 | US 1975-642975 | 19751222 |
| PRIORITY APPLN. INFO.: GI | | | US 1975-642975 | A 19751222 |



I



II

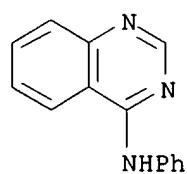
AB Aminoquinazolines I (R = H, Me, Ph, R1 = H, Cl) were prepared in 44-79% yield by treating isatoic anhydrides II with NH₃, followed by POCl₃ and RNH₂.

IT 34923-95-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

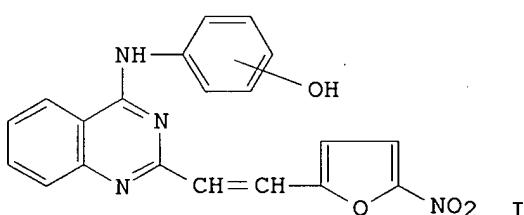
RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 228 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1977:16693 HCPLUS
 DOCUMENT NUMBER: 86:16693
 TITLE: 2-[2-(5-Nitro-2-furyl)vinyl]-4-(hydroxyanilino)quinazolines
 INVENTOR(S): Horn, Herman; Greenbaum, Sheldon B.; Ely, Charles M.; Hacke, Walter; Olle, David A.
 PATENT ASSIGNEE(S): Diamond Shamrock Corp., USA
 SOURCE: U.S., 9 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------------|-----------------|-------------|
| US 3970648 | A | 19760720 | US 1974-503854 | 19740906 |
| US 3973021 | A | 19760803 | US 1975-567499 | 19750414 |
| US 3974277 | A | 19760810 | US 1975-570645 | 19750423 |
| PRIORITY APPLN. INFO.: | | US 1974-503854 | | A3 19740906 |
| GI | | | | |



AB The title compds. I, bactericides and growth promoters for chicks, and the bactericidal anilino analog were prepared from the 4-chloroquinazoline analog. Thus, 9.05 g the 4-chloro analog of I, prepared by chlorination of the condensation product of 5-nitro-2-furancarboxaldehyde and 2-methyl-4(3H)quinazolinone, and 8 g 4-H2NC6H4OH in DMF was heated 2 hr at 70-90° to give 6-5 g I (OH in 4-position).

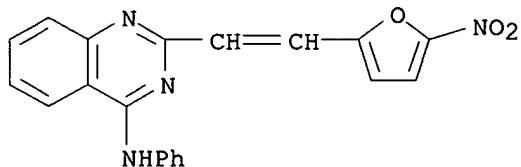
IT 60535-07-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

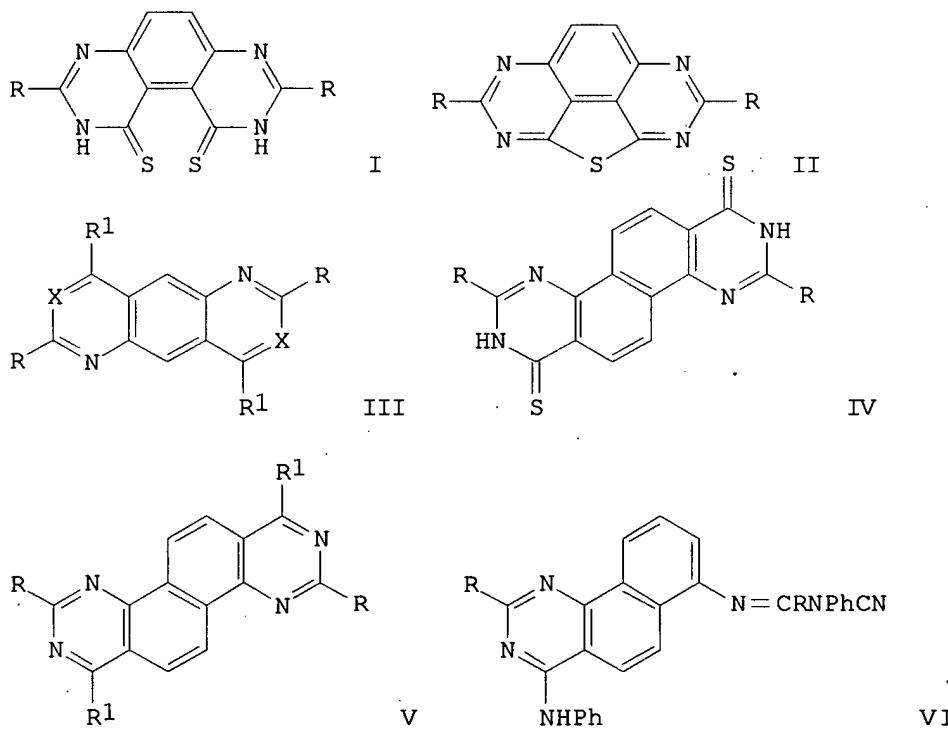
(preparation and bactericidal activity of)

RN 60535-07-1 HCPLUS

CN 4-Quinazolinamine, 2-[2-(5-nitro-2-furyl)ethenyl]-N-phenyl- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1976:592660 HCPLUS
 DOCUMENT NUMBER: 85:192660
 TITLE: Tautomerism of heterocyclic compounds, VI. Synthesis and reactions of bifunctional chloroformamidines
 AUTHOR(S): Ried, Walter; Kothe, Norbert; Schweitzer, Reinhard; Hoehle, Albrecht
 CORPORATE SOURCE: Inst. Org. Chem., Univ. Frankfurt/Main, Frankfurt/Main, Fed. Rep. Ger.
 SOURCE: Chemische Berichte (1976), 109(8), 2921-7
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 OTHER SOURCE(S): CASREACT 85:192660
 GI



AB Ureas (RCONH_2Z (R = morpholino throughout, Z = $\text{p-C}_6\text{H}_4$, 1,5-naphthalenediyl) were converted into 80-58 chloroformamidines ($\text{RCCl:N}_2\text{Z}$ with $\text{PPh}_3\text{-CCl}_4$.

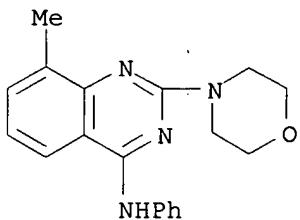
$\text{P-(RCCl:N)}_2\text{C}_6\text{H}_4$ reacted with KNCS , LiC.tplbond.CPh , or PhNHNC to give annulated heterocycles I, which cyclized to 65% II, or III ($\text{R}1 = \text{Ph}$, $\text{X} = \text{CH}$; $\text{R}1 = \text{NHPH}$, $\text{X} = \text{N}$) (12 or 6% yield). ($\text{RCCl:N}_2\text{Z}$ ($\text{Z} = 1,5\text{-naphthalenediyl}$) with KNCS gave 83% IV, which was methylated to 81% V ($\text{R}1 = \text{SMe}$), with PhNHNC gave 58% VI, which cyclized to 45% V ($\text{R}1 = \text{NHPH}$), and with $\text{R}_2\text{C}(\text{NH}_2)\text{:NCN}$ ($\text{R}2 = \text{Ph}$, CCl_3) gave 41 and 12% V ($\text{R}1 = \text{N:CR}_2\text{NH}_2$).

IT 60973-40-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 60973-40-2 HCPLUS

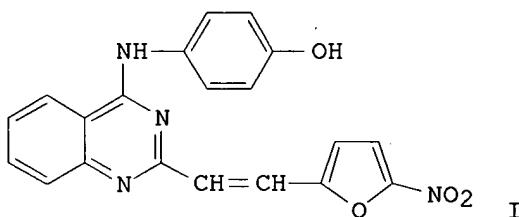
CN 4-Quinazolinamine, 8-methyl-2-(4-morpholinyl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 230 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1976:558452 HCPLUS
 DOCUMENT NUMBER: 85:158452
 TITLE: 2-[2-(5-Nitro-2-furyl)vinyl]-4-(p-hydroxyanilino)quinazoline as a bactericide
 INVENTOR(S): Horn, Herman; Greenbaum, Sheldon B.; Ely, Charles M.; Hacke, Walter; Olle, David A.
 PATENT ASSIGNEE(S): Diamond Shamrock Corp., USA
 SOURCE: U.S., 9 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 3973021 | A | 19760803 | US 1975-567499 | 19750414 |
| US 3970648 | A | 19760720 | US 1974-503854 | 19740906 |
| PRIORITY APPLN. INFO.: | | | US 1974-503854 | A3 19740906 |

GI

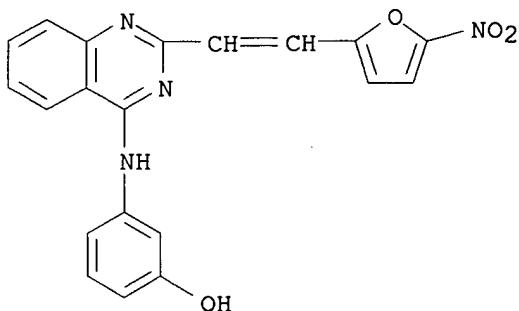


AB 2-[2-(5-Nitro-2-furyl)vinyl]-4-(p-hydroxyanilino)quinazoline (I) [60452-41-7] and similar quinazolines are effective as bactericides and animal growth promoting agents. Thus, broiler chicks given I at 200 g/ton of feed gained 6.5% more weight than controls fed the basal ration plus bacitracin in 4-week expts.; bacitracin plus chlortetracycline at 4 and 200 g/ton, resp. gave only 5.5% better growth, as compared to controls.. Feed efficiency also was improved with addition of I by 7.2% as compared to 6.6% with chlortetracycline.

IT 60452-42-8P
 RL: PREP (Preparation)
 (preparation and feeding experiment on chicks with)

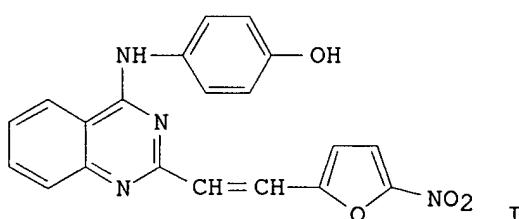
RN 60452-42-8 HCPLUS

CN Phenol, 3-[[2-(5-nitro-2-furyl)ethenyl]-4-quinazolinyl]amino]- (9CI)
 (CA INDEX NAME)



L6 ANSWER 231 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1976:541790 HCPLUS
 DOCUMENT NUMBER: 85:141790
 TITLE: 2-[2-(5-Nitro-2-furyl)vinyl]-4-(anilino)quinazolines
 as growth promotants and feed efficiency enhancing
 agents
 INVENTOR(S): Horn, Herman; Greenbaum, Sheldon B.; Ely, Charles M.;
 Hacke, Walter; Olle, David A.
 PATENT ASSIGNEE(S): Diamond Shamrock Corp., USA
 SOURCE: U.S., 10 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------------------|------|----------|-----------------|-------------|
| US 3974277 | A | 19760810 | US 1975-570645 | 19750423 |
| US 3970648 | A | 19760720 | US 1974-503854 | 19740906 |
| PRIORITY APPLN. INFO.: US 1974-503854 | | | | A3 19740906 |
| GI | | | | |

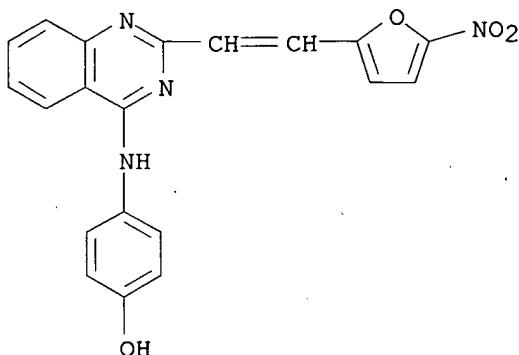


AB The title compds. and derivs. are prepared and found useful as bactericides and animal growth promotants. For example, 2-[2-(5-nitro-2-furyl)vinyl]-4-(p-hydroxyanilino)quinazoline (I) [60452-41-7], prepared by reacting 2-[2-(5-nitro-2-furyl)vinyl]-4-chloroquinazoline [36952-05-3] with p-aminophenol [123-30-8], when added at 200 g/ton to a com.-type chick starter ration containing 4 g bacitracin/ton, increased 4-week growth and feed efficiency to 106 and 107%, resp., of that obtained from the com. diet + bacitracin alone.

IT 60452-41-7P

RL: PREP (Preparation)
 (preparation and bactericidal and animal growth promotant properties of)

RN 60452-41-7 HCPLUS

CN Phenol, 4-[[2-[2-(5-nitro-2-furanyl)ethenyl]-4-quinazolinyl]amino]- (9CI)
(CA INDEX NAME)

L6 ANSWER 232 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1976:463018 HCPLUS

DOCUMENT NUMBER: 85:63018

TITLE: Novel one-pot synthesis of 4-aminoquinazolines

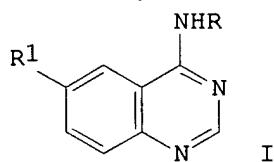
AUTHOR(S): Foster, Charles H.; Elam, Edward U.

CORPORATE SOURCE: Tennessee Eastman Co., Div., Eastman Kodak Co.,
Kingsport, TN, USASOURCE: Journal of Organic Chemistry (1976), 41(15), 2646-7
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

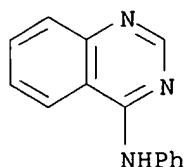
AB The 4-aminoquinazolines I ($R = H, Ph, Me$; $R1 = H, Cl$) were prepared (44-79%) by sequential addition of NH_3 , $POCl_3$, and RNH_2 to a DMF solution of isatoic anhydride or a substituted isatoic anhydride.

IT 34923-95-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

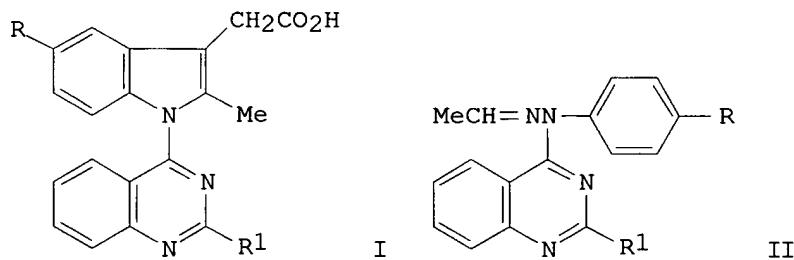
RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 233 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1976:135715 HCAPLUS
 DOCUMENT NUMBER: 84:135715
 TITLE: Quinazolylindoleacetic acids
 PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd., UK
 SOURCE: Fr. Demande, 15 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------|------|----------|-----------------|------------|
| FR 2259613 | A2 | 19750829 | FR 1975-3262 | 19750203 |
| GB 1460348 | A | 19770106 | GB 1974-5015 | 19750102 |
| ZA 7500134 | A | 19760128 | ZA 1975-134 | 19750107 |
| AU 7577240 | A | 19760715 | AU 1975-77240 | 19750110 |
| BE 825128 | A4 | 19750804 | BE 1975-153011 | 19750203 |
| PRIORITY APPLN. INFO.: GI | | | GB 1974-5015 | A 19740204 |



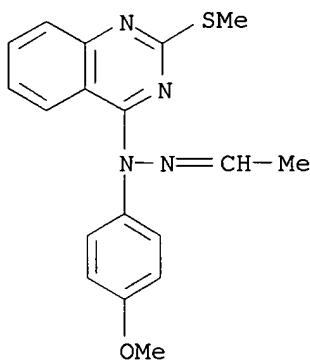
AB Analgesic and antiinflammatory (no data) quinazolylindoleacetic acids I ($R = \text{OMe}$, Me , H , $R1 = \text{SMe}$; $R = \text{OMe}$, $R1 = \text{SET}$) were prepared by treating the 4-chloroquinazolines with $\text{MeCH:NNHC}_6\text{H}_4\text{R}-4$ and cyclizing II with levulinic acid.

IT 58803-72-8P

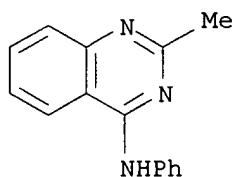
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and condensation of, with levulinic acid)

RN 58803-72-8 HCAPLUS

CN Acetaldehyde, (4-methoxyphenyl)[2-(methylthio)-4-quinazolinyl]hydrazone
 (9CI) (CA INDEX NAME)



L6 ANSWER 234 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1976:43974 HCAPLUS
 DOCUMENT NUMBER: 84:43974
 TITLE: Synthesis and study of the biological activity of substituted 4-amino-2-styrylquinazolines
 AUTHOR(S): Yakhontov, L. N.; Zhikhareva, G. P.; Pronina, E. V.; Pershin, G. N.; Liberman, S. S.; Padeiskaya, E. N.; Zykova, T. N.; Gus'kova, T. A.; Berlyand, E. A.
 CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst. im. Ordzhonikidze, Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1975), 9(11), 12-18
 CODEN: KHFZAN; ISSN: 0023-1134
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 OTHER SOURCE(S): CASREACT 84:43974
 GI For diagram(s), see printed CA Issue.
 AB Aminostyrylquinazolines [I, R = Cl, H, NR₁R₂ = Et₂N, PhNH, PhCH₂NH, Et₂N(CH₂)₃CHMeNH, piperidino, R₃ = o-, p-Cl, p-O₂N] were obtained in 28-66% yields in 5 steps from anthranilic acid derivs. by cyclocondensation with Ac₂O, treatment with NH₃ to give II, chlorination with POCl₃, amination with R₁R₂NH, and condensation with the corresponding aromatic aldehyde. I were effective bactericides against Mycobacterium tuberculosis at 0.25-0.5 µg/ml.
 IT 57942-18-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (condensation of, with aromatic aldehydes)
 RN 57942-18-4 HCAPLUS
 CN 4-Quinazolinamine, 2-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 235 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:72914 HCAPLUS
 DOCUMENT NUMBER: 82:72914
 TITLE: Synthesis and spectral study of 2-phenyl-4-(3'-N-N-

dimethylaminomethyl-4'-hydroxyanilino)+quinazoline derivatives

AUTHOR(S): Patel, J. G.; Bhide, B. H.; Patel, S. R.
 CORPORATE SOURCE: Dep. Chem., Sardar Patel Univ., Vallabh Vidyanagar, India
 SOURCE: Journal of the Indian Chemical Society (1974), 51(7), 674-6

DOCUMENT TYPE: Journal
 LANGUAGE: English

GI For diagram(s), see printed CA Issue.

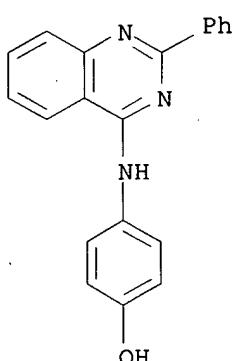
AB The quinazolines I ($R = Et_2NCH_2$, Me_2NCH_2 , piperidinomethyl) were prepared by Mannich reaction of I ($R = H$) with amines. I ($R = H$) was prepared by condensation of $p-HOC_6H_4NH_2$ with 4-chloroquinazolines. The uv spectra of I were determined to check for tautomerism; no conclusion was drawn.

IT 54665-94-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and Mannich reaction of)

RN 54665-94-0 HCPLUS

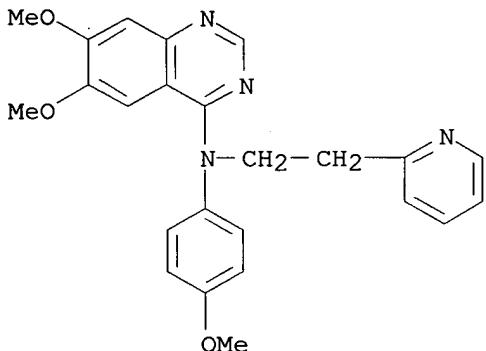
CN Phenol, 4-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 236 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:31349 HCPLUS
 DOCUMENT NUMBER: 82:31349
 TITLE: Quinazoline derivatives
 INVENTOR(S): Barnish, Ian T.; Cox, David Alexander; Evans, Anthony Garth
 PATENT ASSIGNEE(S): Pfizer Corp.
 SOURCE: Ger. Offen., 24 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|-------|----------|-----------------|----------|
| DE 2410938 | ----- | 19740919 | DE 1974-2410938 | 19740307 |
| FR 2220265 | ----- | | FR | |
| GB 1417029 | ----- | | GB | |
| JP 50029582 | ----- | 19750325 | JP 1974-25782 | 19740307 |
| NL 7403075 | ----- | | NL | |
| US 3971783 | ----- | 19760727 | US 1974-464673 | 19740426 |

PRIORITY APPLN. INFO.: GB 1973-11018 19730307
 GI For diagram(s), see printed CA Issue.
 AB Cardiac stimulant aminoquinazolines I [R = H, Me, CH₂Ph, Et, Bu, Pr, C₆H₄OMe-p, CH₂OH; X = CH₂CH₂, (CH₂)₃, CH₂CHMe, CHMeCH₂, (CH₂)₄, CH₂; R₁ = 2-pyridyl, 4-pyridyl, 3-pyridyl, 5-ethyl-2-pyridyl, 4-methyl-2-pyridyl, 6-methyl-2-pyridyl, 2-methyl-4-thiazolyl, 4-imidazolyl, 4-methyl-5-thiazolyl, 2-quinolyl, 2-pyrazinyl, 2-hydroxy-4-methyl-3-pyridyl, 3-indolyl; R₂ = H, Me, OMe; R₃ = OMe, H, OH, NH₂; R₄ = OMe, Cl; R₅ = H, Me, Et, CHMe₂, Cl, CH₂OMe] (43 compds.) were prepared by aminating 4-chloroquinazolines.
 IT 55496-32-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 55496-32-7 HCPLUS
 CN 4-Quinazolinamine, 6,7-dimethoxy-N-(4-methoxyphenyl)-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

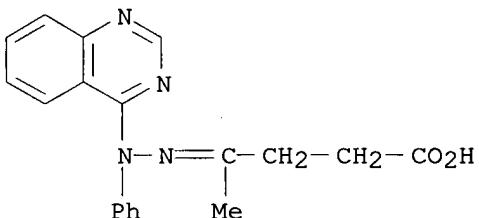


L6 ANSWER 237 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:4289 HCPLUS
 DOCUMENT NUMBER: 82:4289
 TITLE: 1-(4-Quinazolinyl)-3-indoleacetic acids
 INVENTOR(S): Doyle, Martin; Smith, Stephen Collyer
 PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.
 SOURCE: Ger. Offen., 17 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| DE 2410699 | A1 | 19740912 | DE 1974-2410699 | 19740306 |
| GB 1407658 | A | 19750924 | GB 1973-10736 | 19740204 |
| ES 423958 | A1 | 19760516 | ES 1974-423958 | 19740206 |
| NL 7402369 | A | 19740910 | NL 1974-2369 | 19740221 |
| DK 134403 | B | 19761101 | DK 1974-1020 | 19740226 |
| BE 811657 | A1 | 19740827 | BE 1974-141465 | 19740227 |
| DD 110273 | A5 | 19741212 | DD 1974-176929 | 19740304 |
| PL 91000 | B1 | 19770228 | PL 1974-169242 | 19740304 |
| FR 2220528 | A1 | 19741004 | FR 1974-7494 | 19740305 |
| AT 7401823 | A | 19760415 | AT 1974-1823 | 19740305 |
| AT 333747 | B | 19761210 | | |
| JP 50058083 | A | 19750520 | JP 1974-26098 | 19740306 |

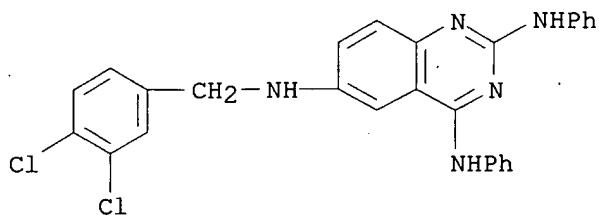
| | | | | |
|------------------------|----|----------|----------------|------------|
| CH 612175 | A5 | 19790713 | CH 1975-998 | 19750128 |
| US 4022780 | A | 19770510 | US 1976-679224 | 19760422 |
| PRIORITY APPLN. INFO.: | | | GB 1973-10736 | A 19730306 |
| | | | US 1974-441389 | A 19740211 |

- GI For diagram(s), see printed CA Issue.
 AB Seven acids I ($R = H$, MeO , or e ; $R1 = H$, Cl-7, Me-2, or $SMe-2$), useful as analgesics, antipyretics, and inflammation inhibitors (no data) were prepared by reaction of $4-RC_6H_4NR_2N:CMeCH_2CH_2CO_2H$ (II, $R2 = H$) with 4-chloroquinazolines, followed by cyclization. Thus, II ($R = MeO$, $R2 = H$) reacted with 4,7-dichloroquinazoline in $MeOCH_2CH_2OMe$ in the presence of HCl in Me_2CHOH at room temperature to give II.HCl ($R = MeO$, $R2 = 7$ -chloro-4-quinazolinyl), which was refluxed in $PhMe$ containing $ZnCl_2$ to give I ($R = MeO$, $R1 = 7$ -Cl).
 IT 54367-24-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclization of)
 RN 54367-24-7 HCPLUS
 CN Pentanoic acid, 4-(phenyl-4-quinazolinylhydrazone)-, hydrochloride (9CI)
 (CA INDEX NAME)



● x HCl

- L6 ANSWER 238 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:89 HCPLUS
 DOCUMENT NUMBER: 82:89
 TITLE: Inhibition of mammalian dihydrofolate reductase by selected 2,4-diaminoquinazolines and related compounds
 AUTHOR(S): Richter, W. E., Jr.; McCormack, J. J.
 CORPORATE SOURCE: Coll. Med., Univ. Vermont, Burlington, VT, USA
 SOURCE: Journal of Medicinal Chemistry (1974), 17(9), 943-7
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Several of the 65 substituted diaminopyridopyrimidines, diaminopteridines, and diaminoquinazolines tested were active inhibitors of dihydrofolate reductase [9002-03-3] from rat liver and L1210 mouse leukemia cells. 2,4-Diamino-6-[(3,4-dichlorobenzyl)methylamino]quinazoline (I) [53274-32-1] was as active an inhibitor of the rat liver reductase as methotrexate [59-05-2]. Structure-activity relations were discussed.
 IT 38918-13-7
 RL: BIOL (Biological study)
 (dihydrofolate reductase inhibition by)
 RN 38918-13-7 HCPLUS
 CN 2,4,6-Quinazolinetriamine, N6-[(3,4-dichlorophenyl)methyl]-N2,N4-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 239 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1974:438929 HCAPLUS

DOCUMENT NUMBER: 81:38929

TITLE: Azo pigment

INVENTOR(S): Mory, Rudolf; Mueller, Rolf

PATENT ASSIGNEE(S): Ciba-Geigy A.-G.

SOURCE: Ger. Offen., 32 pp.

CODEN: GWXXBX

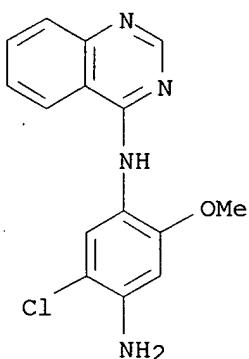
DOCUMENT TYPE: Patent

LANGUAGE: German

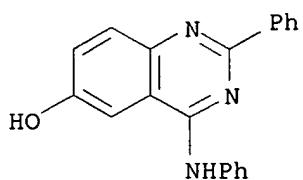
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|---------------|-----------------|----------|
| DE 2341148 | A1 | 19740228 | DE 1973-2341148 | 19730814 |
| CH 579614 | A5 | 19760915 | CH 1972-12197 | 19720817 |
| CA 1008850 | A1 | 19770419 | CA 1973-177797 | 19730731 |
| US 3897411 | A | 19750729 | US 1973-385617 | 19730803 |
| IT 995191 | B | 19751110 | IT 1973-27907 | 19730814 |
| JP 49059836 | A | 19740611 | JP 1973-91642 | 19730815 |
| GB 1405358 | A | 19750910 | GB 1973-38664 | 19730816 |
| ES 417907 | A1 | 19760616 | ES 1973-417907 | 19730816 |
| FR 2196374 | A1 | 19740315 | FR 1973-29965 | 19730817 |
| PRIORITY APPLN. INFO.: | | CH 1972-12197 | A | 19720817 |
| | | CH 1973-10018 | A | 19730710 |
| AB | Coupling of diazotized 4-[(2-methoxy-4-amino-5-chlorophenyl)amino]quinazoline with 1-methyl-5-(acetoacetylarnino)benzimidazolone gave the azo pigment (I) [51817-95-9], migration- and lightfast orange in PVC [9002-86-2]. | | | |
| IT | 51829-62-0
RL: USES (Uses)
(coupling of diazotized, with acetoacetamidomethylbenzimidazolone) | | | |
| RN | 51829-62-0 HCAPLUS | | | |
| CN | 1,4-Benzenediamine, 5-chloro-2-methoxy-N1-4-quinazolinyl- (9CI) (CA INDEX NAME) | | | |

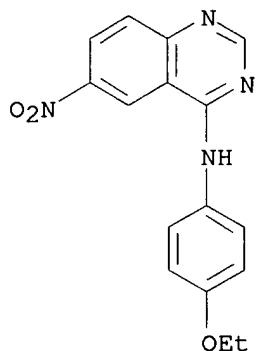


L6 ANSWER 240 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1974:403870 HCPLUS
 DOCUMENT NUMBER: 81:3870
 TITLE: Heterocyclic quinones. XXII. Synthesis and antimicrobial action of substituted 2-phenylquinazolinequinones
 AUTHOR(S): Karpova, N. B.; Tsizin, Yu. S.; Rudzit, E. A.; Radkevich, T. P.; Kulikova, D. A.; Luk'yanov, A. V.
 CORPORATE SOURCE: Inst. Med. Parazitol. Trop. Med. im. Martsinovskogo, Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1974), 8(2), 21-4
 CODEN: KHFZAN; ISSN: 0023-1134
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI For diagram(s), see printed CA Issue.
 AB The quinazolinols I (R = Me₂N, PhNH, MeNH) were oxidized by O in MeOH containing copper acetate and R₁H (R₁ = morpholino, piperidino) to give the corresponding quinazolinediones II. Reduction of II (R = R₁ = piperidino) by Zn in refluxing Ac₂O-pyridine gave the diacetoxyquinazoline III. II (R = MeNH, R₁ = piperidino; R = R₁ = piperidino) possessed antibacterial activity at 0.19-25 µg/ml. Seven isomeric quinazolinediones IV (R = MeO, piperidino; R₁ = HO, MeO, BuNH, MeNH, piperidino, morpholino) were tested for antibacterial activity and IV (R = HO, R₁ = piperidino) was effective at ≥6.25 µg/ml.
 IT 34637-65-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (oxidation-amination of)
 RN 34637-65-5 HCPLUS
 CN 6-Quinazolinol, 2-phenyl-4-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 241 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1974:70768 HCPLUS
 DOCUMENT NUMBER: 80:70768
 TITLE: Synthesis of certain nitroquinazoline derivatives

AUTHOR(S): structurally related to some chemotherapeutic agents
 Botros, S.; Ghoneim, K. M.; Khalifa, M.
 CORPORATE SOURCE: Fac. Pharm., Cairo Univ., Cairo, Egypt
 SOURCE: Egyptian Journal of Pharmaceutical Sciences (1972),
 13(1), 11-21
 CODEN: EJPSBZ; ISSN: 0301-5068
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Aminoquinazolines I [R = Me, Et, Pr, Bu, CH₂CH₂OH, p-R₁-C₆H₄ (R₁ = OH, OEt, CO₂Et, CO₂Et, Br, 6-nitro-4-quinazolinylamino), 6-nitro-4-quinazolinylaminoethyl, 3,4-R₂CH₂(HO)-C₆H₃ (R₂ = NEt₂, piperidino, morpholino)] were prepared by treating 4-chloro-6-nitroquinazoline with the amine.
 IT 51687-12-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 51687-12-8 HCAPLUS
 CN 4-Quinazolinamine, N-(4-ethoxyphenyl)-6-nitro- (9CI) (CA INDEX NAME)



L6 ANSWER 242 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1974:51 HCAPLUS
 DOCUMENT NUMBER: 80:51
 TITLE: Analgesic compounds with no narcotic activity. Study
 of new 4-(2'-alkoxycarbonyl phenylamino) quinolines
 and related molecules
 AUTHOR(S): Allais, A.; Rousseau, G.; Meier, J.; Nomine, G.;
 Peterfalvi, M.; Deraedt, R.; Chifflet, L.; Benzoni,
 J.; Fournex, R.
 CORPORATE SOURCE: Cent. Rech., Roussel-Uclaf, Romainville, Fr.
 SOURCE: Chimica Therapeutica (1973), 8(2), 154-68
 DOCUMENT TYPE: Journal
 LANGUAGE: French
 AB The analgesic activity in acetic acid-treated mice and the
 antiinflammatory activity in rats with β -naphthoylheparamine-induced
 hind paw edema was determined for 156 4-(2-alkoxycarbonylphenylamino)quinolines
 (I). With respect to substituents on the quinoline nucleus, electron
 attracting groups at 7 and 8 enhanced the activity and electron donating
 groups decreased it. Modification of the quinoline structure, such as
 insertion of heterocyclic N atoms suppressed both activities.
 Esterification of the 2'-carboxyl group with glycerol resulted in best
 analgesic activity. Changing the 2'-carboxyl into nitrile, amides,
 hydroxamic derivs. and tetrazoles eliminated almost all the analgesic
 activity, whereas products of alcohol or aldehyde reduction retained some

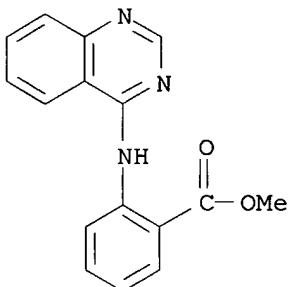
activity. Replacement of the anthranilic nucleus by certain simple thiophenes resulted in compds. with strong analgesic activity, sometimes accompanied by marked antiinflammatory activity.

IT 49712-49-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic and antiinflammatory activities of)

RN 49712-49-4 HCAPLUS

CN Benzoic acid, 2-(4-quinazolinylamino)-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 243 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1973:542776 HCAPLUS

DOCUMENT NUMBER: 79:142776

TITLE: Potential antitumor agents. 13. Bisquaternary salts

AUTHOR(S): Atwell, G. J.; Cain, B. F.

CORPORATE SOURCE: Cancer Chemother. Lab., Cornwall Geriatr. Hosp.,
Auckland, N. Z.SOURCE: Journal of Medicinal Chemistry (1973), 16(6), 673-8
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

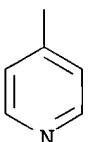
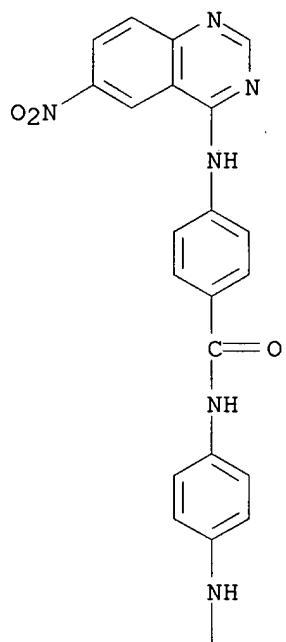
AB 4-Anilinoquinolinium compounds bearing any of a number of quaternary N substituents on the phenyl ring were active in mice against L1210 leukemia. Activity was enhanced by the electron-donor substituents such as an amino group on the quinoline nucleus, as in 6-amino-1-ethyl-4-[p-[p-[(1-ethylpyridinium-4-yl)amino]phenylcarbamoyl]anilino]quinolinium dibromide (I) [42013-69-4], or by a 7-nitro group. I at 0.67 mg/kg/day i.p. for 5 days, given to mice inoculated i.p. with 105 L1210 cells 1 day previously, increased the life span by 40% and 2 out of 6 inoculated mice survived for 100 days when treated with 6.7 mg I/kg/day for 5 days. This survival indicated a lower toxicity of I (and of several related compds. tested) and of some bisquaternary antileukemics reported previously. I was prepared by condensation of 4-chloro-1-ethyl-6-nitroquinolinium [42013-70-7], prepared from 6-nitro-4-hydroxyquinoline [23432-42-0], with 1-ethyl-4-[4-(4-aminobenzamido)anilino]pyridinium [42013-72-9], followed by a reduction of the NO₂ group to NH₂.

IT 50440-33-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)

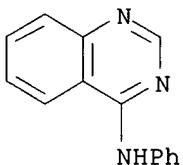
RN 50440-33-0 HCAPLUS

CN Benzamide, 4-[(6-nitro-4-quinazolinyl)amino]-N-[4-(4-pyridinylamino)phenyl]- (9CI) (CA INDEX NAME)

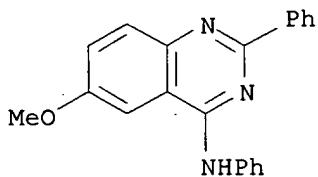


L6 ANSWER 244 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:537083 HCPLUS
 DOCUMENT NUMBER: 79:137083
 TITLE: Vilsmeier-Haack reaction. VI. Reaction with isatin
 β -oxime and a convenient synthesis of
 o-aminobenzonitriles, 4-aminoquinazolines, and
 4-aminoquinazoline 3-oxides
 AUTHOR(S): Deshpande, M. N.; Seshadri, S.
 CORPORATE SOURCE: Dep. Chem. Technol., Univ. Bombay, Bombay, India
 SOURCE: Indian Journal of Chemistry (1973), 11(6), 538-40
 CODEN: IJOCAP; ISSN: 0019-5103
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Isatin β -oxime (I) underwent a transformation with the Vilsmeier
 reagent (DMF-POCl₃) yielding N,N-dimethyl - N' - (o-
 cyanophenyl)formamidine. Substituted isatin oximes underwent similar
 reactions. The formamidine derivs. were characterized by their ir spectra
 and by hydrolysis to corresponding o-aminobenzonitriles. The formamidine
 derivs. were readily converted into 4-aminoquinazoline derivs. II (R = H,
 R₁ = H, NO₂, Br; R = R₁ = Br) using NH₄OAc and into 4-aminoquinazoline
 3-oxides by reaction with NH₂OH.HCl.

IT 34923-95-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 34923-95-0 HCAPLUS
 CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 245 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:492149 HCAPLUS
 DOCUMENT NUMBER: 79:92149
 TITLE: Synthesis and antimicrobial action of N-substituted 2-phenyl-4-amino-6-hydroxyquinazolines
 AUTHOR(S): Tsizin, Yu. S.; Karpova, N. B.; Luk'yanov, A. V.;
 Rudzit, E. A.; Kulikova, D. A.; Radkevich, T. P.
 CORPORATE SOURCE: Inst. Med. Parazitol. Trop. Med. im. Martsinovskogo,
 Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1973), 7(7), 16-19
 CODEN: KHFZAN; ISSN: 0023-1134
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI For diagram(s), see printed CA Issue.
 AB Seventeen 2-phenyl-6-quinazolinols [I; R1 = PhNH, p-MeOC6H4NH, m-,
 p-ClC6H4NH, MeNH, Me2N, Me(CH2)11NH, piperidino, morpholino,
 4-methyl-1-piperazinyl, NH2, H, OH, OMe; R2 = H, OH, OMe] were prepared by
 known methods and their bactericidal activity determined. I (R1 = Me2N, R2 =
 OH) was effective against diphtheria, staphylococcus, and anthrax at
 1.56-3.12 µg/ml while I (R1 = BuNH, R2 = OH) was effective against
 tuberculosis at 0.39-0.78 µg/ml.
 IT 34637-61-1
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (bactericidal activity of)
 RN 34637-61-1 HCAPLUS
 CN 4-Quinazolinamine, 6-methoxy-N,2-diphenyl- (9CI) (CA INDEX NAME)

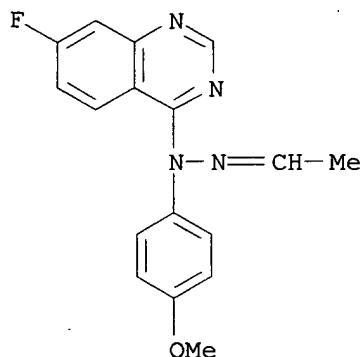


L6 ANSWER 246 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:431865 HCAPLUS
 DOCUMENT NUMBER: 79:31865
 TITLE: Indole derivatives
 INVENTOR(S): Birchall, George Richard; Hepworth, Walter; Smith,
 Stephen Collyer
 PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.

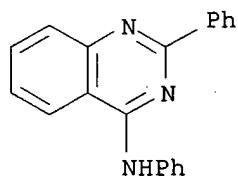
SOURCE: Ger. Offen., 126 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------------|-----------------|----------|
| DE 2253927 | A1 | 19730510 | DE 1972-2253927 | 19721103 |
| GB 1356834 | A | 19740619 | GB 1972-18116 | 19720419 |
| CA 983932 | A1 | 19760217 | CA 1972-152944 | 19720929 |
| ZA 7207007 | A | 19730627 | ZA 1972-7007 | 19721002 |
| AU 7247381 | A | 19740411 | AU 1972-47381 | 19721004 |
| IL 40521 | A | 19750625 | IL 1972-40521 | 19721006 |
| US 3884919 | A | 19750520 | US 1972-296202 | 19721010 |
| SU 527135 | A3 | 19760830 | SU 1972-1843832 | 19721020 |
| BE 790679 | A1 | 19730427 | BE 1972-123586 | 19721027 |
| NL 7214807 | A | 19730507 | NL 1972-14807 | 19721102 |
| FR 2158464 | A1 | 19730615 | FR 1972-38836 | 19721102 |
| JP 48056667 | A | 19730809 | JP 1972-110172 | 19721102 |
| DD 105611 | A5 | 19740512 | DD 1972-166646 | 19721102 |
| SE 384856 | B | 19760524 | SE 1972-14215 | 19721102 |
| CH 577499 | A5 | 19760715 | CH 1972-15976 | 19721102 |
| AT 320633 | B | 19750225 | AT 1972-9342 | 19721103 |
| AT 7401001 | A | 19750615 | AT 1972-100174 | 19721103 |
| AT 7401002 | A | 19750615 | AT 1972-100274 | 19721103 |
| AT 7401003 | A | 19750615 | AT 1972-100374 | 19721103 |
| ES 408226 | A1 | 19760201 | ES 1972-408226 | 19721103 |
| HU 169711 | B | 19770228 | HU 1972-IE540 | 19721103 |
| CS 178144 | B2 | 19770831 | CS 1972-548 | 19721103 |
| CS 178120 | B2 | 19770831 | CS 1972-7437 | 19721103 |
| SU 577980 | A3 | 19771025 | SU 1974-2043161 | 19740711 |
| US 4012513 | A | 19770315 | US 1974-535839 | 19741223 |
| ES 437331 | A1 | 19770401 | ES 1975-437331 | 19750430 |
| PRIORITY APPLN. INFO.: | | | | |
| | | GB 1971-51086 | A | 19711103 |
| | | GB 1972-18116 | A | 19720419 |
| | | GB 1972-30767 | A | 19720630 |
| | | US 1972-296202 | A2 | 19721010 |

GI For diagram(s), see printed CA Issue.
 AB Indole derivs. I (e.g. R = CO₂H, CH₂OH, CONH₂; R₁ = 4-quinazolyl, 2-benzothiazolyl, pyrimidinyl, 2-quinolyl, quinoxalinyl; R₂ = H, MeO) were prepared for use as analgesics, antipyretics, and inflammation inhibitors. Thus I (R = CO₂H, R₁ = 2-amino-6-methyl-4-pyrimidinyl, R₂ = H) was obtained by treating 2-amino-4-chloro-6-methylpyrimidine with PhHNHNH₂ and cyclizing with levulinic acid.
 IT 41800-62-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 41800-62-8 HCAPLUS
 CN Acetaldehyde, (7-fluoro-4-quinazolinyl)(4-methoxyphenyl)hydrazone (9CI)
 (CA INDEX NAME)



L6 ANSWER 247 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:136213 HCPLUS
 DOCUMENT NUMBER: 78:136213
 TITLE: Conversion of indoles into quinazolines. New quinazoline synthesis
 AUTHOR(S): Yoneda, Fumio; Higuchi, Masatsugu; Nonaka, Reiko
 CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, Japan
 SOURCE: Tetrahedron Letters (1973), (5), 359-60
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 78:136213
 AB 3-Nitroso-2-phenylindole (I) with excess POCl_3 or $p\text{-MeC}_6\text{H}_4\text{SO}_3\text{H}$ in sulfolane at 200° for 1 hr gave 90 or 68% 2-phenyl-4(3H)-quinazolinone, resp. The reaction proceeds by a second order Beckmann rearrangement of the imino oxime tautomer of I. I with excess POCl_3 and PhNH_2 or PhCH_2NH_2 gave 50 or 65%, resp., of 4-anilino- or 4-(benzylamino)-2-phenylquinazoline.
 IT 40288-70-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 40288-70-8 HCPLUS
 CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 248 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:124529 HCPLUS
 DOCUMENT NUMBER: 78:124529
 TITLE: Reactions of 4-substituted quinazoline with several nucleophilic reagents
 AUTHOR(S): Higashino, Takeo; Ito, Hiroyuki; Watanabe, Masayuki; Hayashi, Eisaku
 CORPORATE SOURCE: Shizuoka Coll. Pharm., Shizuoka, Japan
 SOURCE: Yakugaku Zasshi (1973), 93(1), 94-100
 CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE:

Journal

LANGUAGE:

Japanese

GI For diagram(s), see printed CA Issue.

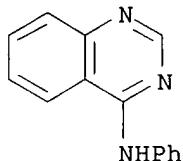
AB In order to examine the reactivity of ring C at 4-position towards nucleophilic reagents, reaction of 4-methoxyquinazoline (I, R = OMe) (II), 2-methyl-2-(4-quinalinyl)-propiophenone (I, R = Me₂COPh) (III) and α -phenyl-4-quinalineacetonitrile, ethyl cyanoacetate, and malononitrile in methanol, in the presence of a methoxide ion, resp. gave IV, and I (R = NCCHCO₂Me, CH(CN)₂). The reaction of III with methoxide ion, aniline, butylamine, piperidine, and hydrazine resp. afforded II and I (R = PhNH, BuNH, piperidino, H₂NNH). The reaction of III with acetone and acetophenone, in the presence of sodium amide gave I (R = CHMe₂) and PhCOCH₂COR (R = Me, Ph, resp.). The reaction of IV with methoxide ion, aniline, butylamine, and piperidine resp. afforded II, I (R = PhNH, piperidino).

IT 34923-95-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 249 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1972:522112 HCPLUS

DOCUMENT NUMBER: 77:122112

TITLE: Antimalarial drugs. 24. Folate antagonists. 2.
2,4-Diamino-6-[{aralkyl and
(heterocyclic)methyl]amino}quinazolines, a novel class
of antimetabolites of interest in drug-resistant
malaria and Chagas' disease

AUTHOR(S): Davoll, John; Johnson, A. M.; Davies, H. J.; Bird, O. D.; Clarke, J.; Elslager, Edward F.

CORPORATE SOURCE: Res. Dev. Div., Parke, Davis and Co.,
Hounslow/Middlesex, UKSOURCE: Journal of Medicinal Chemistry (1972), 15(8), 812-26
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 77:122112

AB 2,4-Diamino-6-[(3-bromobenzyl)amino]quinazoline (I) [36504-76-4], the most potent compound in a series of antimalarial folate antagonists synthesized, had 190 times the activity of quinine-HCl against Plasmodium berghei in mice (90% suppression of parasitemia by 0.4 mg I/kg/day orally).

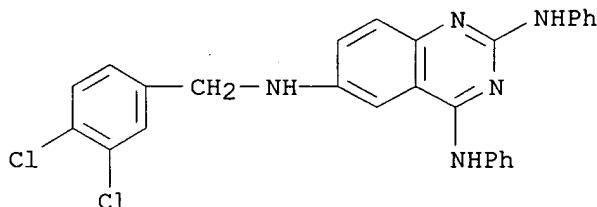
5-Substitution as in 2,4-diamino-5-chloro-6-[(3,4-dichlorobenzyl)amino]quinazoline [17511-29-4], or α -substitution on the benzyl group as in 2,4-diamino-6-[(1-phenylethyl)amino]quinazoline [17593-04-3], enhanced the activity of compds. in the series. Several compds. including 2,4-diamino-6-[(3,4-dichlorobenzyl)amino]quinazoline (II) [13794-65-5] were curative at 100 mg/kg/day against P. cynomolgi in rhesus monkeys. I exhibited strong effects against cycloguanil-, pyrimethamine-, 4,4'-sulfonyldianiline-, and chloroquine-resistant lines of P. berghei. 28 Quinazolines were active against Trypanosoma cruzi in

chick embryo cell cultures at 0.39-6.25 µg/ml, and 5 showed antitrypanosomal effects in mice. Good correlation was observed among the most potent compds. between antimarial activity and antibacterial activity against folate-grown *Streptococcus faecalis* R. I, II, and 8 other quinazolines inhibited growth of methotrexate- and aminopterin-resistant *S. faecalis* A, indicating little cross-resistance. I was synthesized from 2,4-diamino-6-nitroquinazoline by reduction of the nitro group, condensation with 3-bromobenzaldehyde, and reduction of the Schiff base with NaBH4.

IT 38918-13-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(protozoacidal activity of, folic acid antagonism in relation to)

RN 38918-13-7 HCAPLUS

CN 2,4,6-Quinazolinetriamine, N6-[(3,4-dichlorophenyl)methyl]-N2,N4-diphenyl-
(9CI) (CA INDEX NAME)

L6 ANSWER 250 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1972:153706 HCAPLUS

DOCUMENT NUMBER: 76:153706

TITLE: Use of amide chlorides in ring closure reactions. IV.

New synthesis of 4-aminoquinazoline derivatives

AUTHOR(S): Csuros, Zoltan; Soos, R.; Bitter, I.; Palinkas, J.

CORPORATE SOURCE: Org. Chem. Technol. Inst., Tech. Univ., Budapest,
Hung.SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1972),
72(1), 59-64

CODEN: ACASA2; ISSN: 0001-5407

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

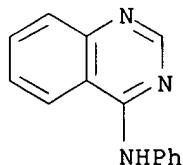
AB The 4-aminoquinazolines I (R = H, Bu, HOCH2CH2, Ph, p-MeC6H4, p-H2NC6H4, NH2) were prepared by cyclizing the formamidinium chloride II with amines RNH2. II was obtained by treating anthranilamide with 2 moles Me2N+:CHCl Cl-.

IT 34923-95-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(ir spectrum)

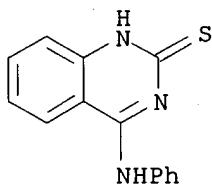
RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 251 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1972:72307 HCAPLUS
 DOCUMENT NUMBER: 76:72307
 TITLE: 1-Methyl-3-phenyl-indans by dimerizing styrenes in the presence of catalysts and polymerization inhibitors
 INVENTOR(S): Armbrust, Herbert; Sturm, Hans J.; Kilpper, Gerhard; Koehler, Waldemar; Schecker, Hans G.
 PATENT ASSIGNEE(S): Badische Anilin- & Soda-Fabrik AG
 SOURCE: Ger. Offen., 14 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| DE 2029026 | A | 19711216 | DE 1970-2029026 | 19700612 |
| DE 2029026 | B2 | 19800731 | | |
| DE 2029026 | C3 | 19810430 | | |
| BE 768410 | A1 | 19711213 | BE 1971-104521 | 19710611 |
| GB 1343445 | A | 19740109 | GB 1971-27416 | 19710611 |
| JP 52012191 | B | 19770405 | JP 1971-41444 | 19710612 |
| PRIORITY APPLN. INFO.: | | | DE 1970-2029026 | A 19700612 |
| AB | The title dimerization with known catalysts, e.g. H ₃ PO ₄ , was tech. feasible in the presence of polymerization inhibitors. Results of runs, continuous and (or) discontinuous, with .apprx.35 polymerization inhibitors were given. | | | |
| IT | 35696-83-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(as polymerization inhibitors in dimerization of styrene) | | | |
| RN | 35696-83-4 HCAPLUS | | | |
| CN | 2(1H)-Quinazolinethione, 4-(phenylamino)- (9CI) (CA INDEX NAME) | | | |



L6 ANSWER 252 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1972:34199 HCAPLUS
 DOCUMENT NUMBER: 76:34199
 TITLE: Synthesis and absorption spectra of 4-aminoquinazoline derivatives
 AUTHOR(S): Bigar, L. I.; Grin, V. A.
 CORPORATE SOURCE: USSR
 SOURCE: Khim. Issled. Farm. (1970) 6-8
 From: Ref. Zh., Khim. 1970, Abstr. No. 22Zh371
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 AB Heating 0.01 mole 4-chloroquinazoline 40-90 min with the appropriate amines (0.011 mole) at .apprx.100° in 50% Me₂CO catalyzed by HCl gave 4-(R-substituted amino)-quinazolines [I, R=NH₂CH₂CH₂, Et₂N(CH₂)₃CHMe,

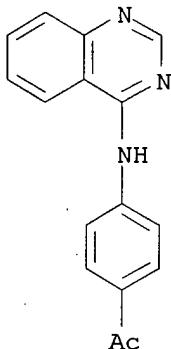
PhCH₂CH₂, Ph, MeC₆H₄, p-ClC₆H₄, p-HOC₆H₄, p-EtC₆H₄, p-MeOC₆H₄, p-H₂NC₆H₄, p-AcC₆H₄, p-O₂NC₆H₄] and their uv spectra were studied. Uv spectra of I were affected by the electron displacements by electron-donor and -acceptor substituents. The amino N atom at the 4 position created the conditions for p, π junctions between the rings while (CH₂)_n groups interrupted them.

IT 19062-70-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19062-70-5 HCAPLUS

CN Ethanone, 1-[4-(4-quinazolinylamino)phenyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 253 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1972:14467 HCAPLUS

DOCUMENT NUMBER: 76:14467

TITLE: Synthesis of substituted 2-phenyl-6-hydroxyquinazolines

AUTHOR(S): Tsizin, Yu. S.; Karpova, N. B.; Efimova, O. V.

CORPORATE SOURCE: Inst. Med. Parazitol. Trop. Med. im. Martsinovskogo, Moscow, USSR

SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1971), 7(3), 418-20

CODEN: KGSSAQ; ISSN: 0132-6244

DOCUMENT TYPE: Journal

LANGUAGE: Russian

GI For diagram(s), see printed CA Issue.

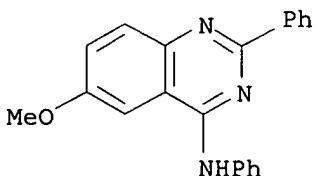
AB 2-Phenyl-6-methoxyquinazolin-4-one (I) was obtained by condensation of benzoyl-p-anisidine with Et urethane. Demethylation of I gave II. II was acetylated and treated with SOC₁₂ to form (III, R = OAc, R₁ = Cl) which, heated with alc. primary and secondary amines gave III (R = OH; R₁ = NET₂, morpholino, BuNH, and PhNH).

IT 34637-61-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 34637-61-1 HCAPLUS

CN 4-Quinazolinamine, 6-methoxy-N,2-diphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 254 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1971:551829 HCAPLUS
 DOCUMENT NUMBER: 75:151829
 TITLE: Diuretic 4-aminoquinazolines.
 INVENTOR(S): Robba, Max F.; Marcy, Rene H. P.; Duval, Denise J. C.
 PATENT ASSIGNEE(S): Innothera
 SOURCE: Ger. Offen., 14 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| DE 2106510 | A | 19710826 | DE 1971-2106510 | 19710211 |
| FR 2077803 | A5 | 19711105 | FR 1970-5371 | 19700216 |
| FR 2077803 | B1 | 19730316 | | |
| US 3772295 | A | 19731113 | US 1971-115797 | 19710216 |
| JP 50010866 | B | 19750424 | JP 1971-6550 | 19710216 |
| GB 1298313 | A | 19721129 | GB 1971-1298313 | 19710419 |
| PRIORITY APPLN. INFO.: | | | FR 1970-5371 | A 19700216 |

GI For diagram(s), see printed CA Issue.

AB 4-Aminoquinazolines (I), useful as natriuretic and chlorouretic agents, were prepared from 4-quinazolones by reaction with POCl₃ to give I (R₁=Cl) and reaction with amines. Thus, 4-quinazolinone was refluxed with POCl₃ and PCl₅ 4 hr to give 72% I (R=R₂=H, R₁=Cl), which was refluxed with m-F₃CC₆H₄NH₂ in absolute EtOH 3 hr to give, after reaction with HO₂CCO₂H, 4-[m-(trifluoromethyl)anilino] quinazoline oxalate [I oxalate (R=R₂=H, R₁=m-F₃CC₆H₄NH₂)]. Similarly prepared were 12 addnl. I. The toxicity of I was tested in mice, e.g. 600 or 900 mg/kg 4-(furfurylamino)-2-(α -thienyl)quinazoline (II) killed 33 or 100% mice, resp., 5 days after i.p. administration. The diuretic activity of I was tested in rats, e.g. 100 mg II/kg increased the urine volume 5.5 fold with respect to that of untreated rats.

IT 34116-11-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

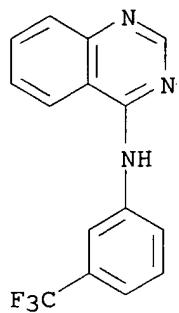
RN 34116-11-5 HCAPLUS

CN Quinazoline, 4-(α , α , α -trifluoro-m-toluidino)-, oxalate
 (8CI) (CA INDEX NAME)

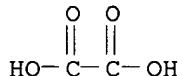
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CRN 47155-57-7

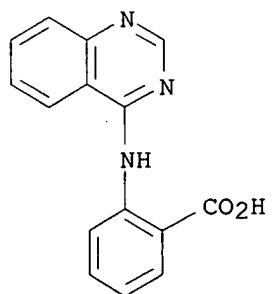
CMF C15 H10 F3 N3



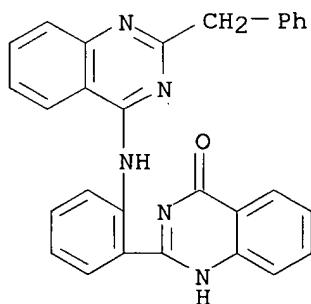
CM 2

CRN 144-62-7
CMF C2 H2 O4

L6 ANSWER 255 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1971:475624 HCPLUS
 DOCUMENT NUMBER: 75:75624
 TITLE: Spectrophotometric examination of N-quinazolyl derivatives of aminobenzoic acid
 AUTHOR(S): Solonskaya, N. T.; Bliznyukov, V. I.
 CORPORATE SOURCE: Kharkov Pharm. Inst., Kharkov, USSR
 SOURCE: Farmatsevtichnii Zhurnal (Kiev) (1971), 26(3), 21-5
 CODEN: FRZKAP; ISSN: 0367-3057
 DOCUMENT TYPE: Journal
 LANGUAGE: Ukrainian
 AB o-, m-, or p-N-(4-quinazolyl)aminobenzoic acids were prepared and their uv spectra studied. The NH group in the ortho and para isomers participated sep. in conjugation with quinazoline and the benzene ring.
 IT 33683-28-2
 RL: PRP (Properties)
 (spectrum of, uv)
 RN 33683-28-2 HCPLUS
 CN Benzoic acid, 2-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

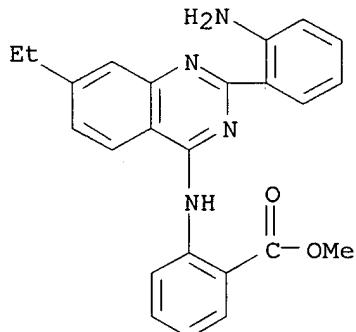


L6 ANSWER 256 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1971:99979 HCPLUS
 DOCUMENT NUMBER: 74:99979
 TITLE: 4-Quinazolinones. II. Self-condensation of anthranilamide
 AUTHOR(S): Pakrashi, Satyesh C.
 CORPORATE SOURCE: Indian Inst. Exp. Med., Calcutta, India
 SOURCE: Journal of Organic Chemistry (1971), 36(5), 642-5
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Condensation of phenylacetic acid with anthranilamide in xylene in presence of phosphorus pentoxide furnished 2-benzyl-4-quinazolinone, o-aminobenzonitrile, tricycloquinazoline (I), 2-(o-aminophenyl)-4-quinazolinone (II), 6,12-diaminophenohomazine (III), and a compound, C₂₉H₂₁N₅O (IV), m. 281°. The mass spectral fragmentation of I, II, and IV are discussed.
 IT 27259-76-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 27259-76-3 HCPLUS
 CN 4(3H)-Quinazolinone, 2-[o-[(2-benzyl-4(3H)-quinazolinylidene)amino]phenyl]- (8CI) (CA INDEX NAME)

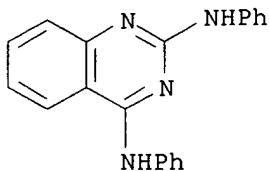


L6 ANSWER 257 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1971:53704 HCPLUS
 DOCUMENT NUMBER: 74:53704
 TITLE: Cyclic amidines. XXII. Novel isomerism of disubstituted tricycloquinazolines and molecular orientations in carcinogenesis
 AUTHOR(S): Partridge, Maurice W.; Brunswick, D. J.; Vipond, H. J.
 CORPORATE SOURCE: Univ. Nottingham, Nottingham, UK
 SOURCE: Journal of the Chemical Society [Section] C: Organic (1970), (19), 2641-7
 CODEN: JSOOAX; ISSN: 0022-4952
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Certain disubstituted tricycloquinazolines, such as I and II, exhibit an unusual structural isomerism originating from the modification of the symmetry of tricycloquinazoline by substitution. Mol. orientations specific for carcinogenesis, consistent with differences in the carcinogenic activities of such isomers and other 2-substituted tri-cycloquinazolines were deduced.
 IT 30380-10-0P

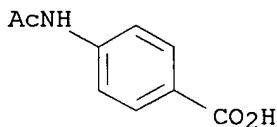
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 30380-10-0 HCPLUS
 CN Anthranilic acid, N-[2-(o-aminophenyl)-7-ethyl-4-quinazolinyl]-, methyl ester (8CI) (CA INDEX NAME)



L6 ANSWER 258 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1970:498888 HCPLUS
 DOCUMENT NUMBER: 73:98888
 TITLE: Synthesis and biological properties of some 2,4-dianilinoquinazoline derivatives
 AUTHOR(S): Brzozowski, Tadeusz; Dymek, Wojciech
 CORPORATE SOURCE: Ist. Dep. Org. Syn., Polska Akad. Nauk, Warsaw, Pol.
 SOURCE: Dissertationes Pharmaceuticae et Pharmacologicae (1970), 22(2-3), 117-25
 CODEN: DPHFAK; ISSN: 0012-3870
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB 2,4-Dianilinoquinazoline, 4-hydroxy-2-anilinoquinazoline, 2-anilino-4-morpholinoquinazoline, 2,4-dihydrazinoquinazoline-HCl, 2-anilino-4-hydrazinoquinazoline, and 9 other compds. were synthesized from 2-anilino-4-chloroquinazoline and 2,4-dichloroquinazoline, and the 1st 3 products had antibacterial action against *Shigella shigae* [S. dysenteriae], *Staphylococcus* 209P, and *Streptococcus pyogenes*, while the latter 2 products inhibited rat brain mitochondrial monoamine oxidase activity.
 IT 28588-40-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 28588-40-1 HCPLUS
 CN Benzoic acid, p-acetamido-, compd. with 2,4-dianilinoquinazoline (1:1) (8CI) (CA INDEX NAME)
 CM 1
 CRN 27142-44-5
 CMF C20 H16 N4



CM 2

CRN 556-08-1
CMF C9 H9 N O3

L6 ANSWER 259 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1970:31830 HCPLUS
 DOCUMENT NUMBER: 72:31830
 TITLE: Bactericidal 4-(o-, m-, and p-hydroxyanilino)-2-(5-nitro-2-furyl)quinazolines
 PATENT ASSIGNEE(S): Norwich Pharmacal Co.
 SOURCE: Brit., 3 pp.
 CODEN: BRXXAA
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| GB 1168430 | | 19691022 | GB 1969-4748 | 19690128 |
| DE 1909522 | | | DE | |
| FR 2005591 | | | FR | |
| US 3542784 | | 19701124 | US | 19680405 |
| ZA 6900771 | | 19690000 | ZA | |

PRIORITY APPLN. INFO.:

GI For diagram(s), see printed CA Issue.

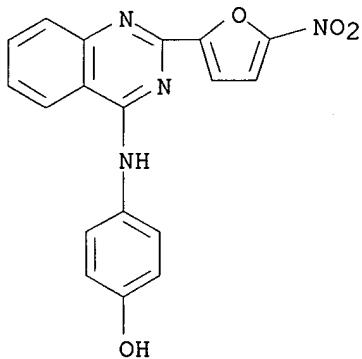
AB The title compds. (I) in which the OH may be in the 2-, 3-, or 4-position show high in vitro antibacterial activity. A mixture of 35 g II and 28.5 g o-HOC₆H₄NH₂ in 500 ml Me₂NCHO was heated on the steam-bath 2 hr to give 35 g I (2-OH) (III), m. 275° (decomposition). Similarly were prepared I (3-OH) (IV), m. 284° (decomposition) and I (4-OH), m. 286-8° (decomposition). I were particularly effective in vitro against animal pathogens.

IT 24912-15-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 24912-15-0 HCPLUS

CN Phenol, p-[[2-(5-nitro-2-furyl)-4-quinazolinyl]amino]- (8CI) (CA INDEX NAME)



L6 ANSWER 260 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1969:491519 HCAPLUS

DOCUMENT NUMBER: 71:91519

TITLE: Hypotensive 2,4-diaminoquinazolines

PATENT ASSIGNEE(S): Pfizer, Chas., and Co., Inc.

SOURCE: Brit., 39 pp.

CODEN: BRXXAA

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------|----------|-----------------|----------|
| GB 1156973 | ----- | 19690702 | GB 1966-29544 | 19660630 |
| DE 1620138 | ----- | | DE | |
| FR 6396 | ----- | | FR | |
| US 3511836 | ----- | 19700512 | US | 19671213 |
| US 3663706 | ----- | 19720516 | US | 19690929 |
| PRIORITY APPLN. INFO.: | | | US | 19650706 |
| | | | US | 19660607 |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) are prepared from II; in I and II, R1 = R2 = MeO unless otherwise indicated. Thus, 30 g. II (Z1 = Z2 = Cl) (IIa) is added to 800 ml. solution of anhydrous NH3 in tetrahydrofuran (THF) at room temperature, and

the mixture stirred 44 hrs. to precipitate 29 g. II (Z1 = Cl, Z2 = NH2) (IIb), m.

302° (decomposition) (MeOH). To 5 g. IIb is added 20 g. 25% 4-methylpiperazine in EtOH, and the mixture heated 16 hrs. at 160° and worked up to give I (Z1 = 4-methylpiperazino, Z2 = NH2) (Ia). A mixture of 7.78 g. IIa and 100 ml. 25% alc. Ph2NH is heated 65 hrs. at 160° and worked up to give I (Z1 = Z2 = Ph2N). To 800 ml. of a solution of Et2NH in THF is added 30 g. IIa, and the mixture stirred 48 hrs. to precipitate II

(Z1 = Cl, Z2 = Et2N). This (5 g.) is heated 16 hrs. at 160° with 25% alc. (PhCH2)2NH to give I [Z1 = (PhCH2)2N, Z2 = Et2N]. A suspension of 11 g. Na cyanate in 50 ml. H2O is stirred 1 hr. with 20 g. 4-amyoxy-5-methoxyanthranilamide in 100 ml. HOAc to give 2-ureido-4-amyoxy-5-methoxybenzamide. This (20 g.) is heated (steam bath) 1 hr. with 50 ml. 8 N HCl and worked up to give I (Z1 = Z2 = OH, R1 = MeO, R2 = n-C5H11O); this (10 g.) is refluxed with 16 g. PCl5 and 10 ml. POC13, and the product distilled to give II (Z1 = Z2 = Cl, R1 = MeO, R2 = n-C5H11O). A mixt of 5 g. IIb and 50 ml. 25% alc. Et2NH is heated 16 hrs. at 160° and worked up to give 3.3 g. I (Z1 = Et2N, Z2 = NH2) (Ib),

m. 179-80° (aqueous MeOH); HCl salt m. 259-60°. IIa (30 g.) is added to 80 g. 10% Me2NH in THF at room temperature, and the mixture stirred 48 hrs. to precipitate (presumably) II (Z1 = Cl, Z2 = Me2N). This (5 g.) is heated

16 hrs. at 160° with 20 g. 10% alc. Me2NH to give (Z1 = Z2 = Me2N), m. 121-2° (aqueous MeOH); HCl salt m. 243°. Similarly prepared is 2-dimethylamino-4-amino-6,7-benzoquinazoline. HBr (22.6 g., 48%) is added over 30 min. to 11.6 g. piperazine in 127 ml. EtOH and 16 ml. H2O (temperature rises to 60°), 8.75 g. ClCO2CHMe2 added over 30 min., and the solution refluxed 30 min. and worked up to give 60% iso-Bu piperazine-1-carboxylate, b. 87-90°/0.3 mm. A mixture of 11.7 g. of this and 7.17 g. IIb in 80 ml. EtOH is heated 4 hrs. at 140° and worked up to give 62% I.HCl (Z1 = 4-isobutoxycar-bonylpiperazino, Z2 = NH2) (Ic), m. 277-8°; the HCl salts, m. 277-8 and 260-2°, resp., of the analogous Et and allyl esters are prepared similarly, as are the following I (Z2 is NH2) (Z1 given): 4-allylpiperazino (Id) [m. 198-201° (unrecrystd.); HCl salt m. 282-3° (unrecrystd.)]; 4-benzylpiperidino [m. 260-2° (1:1 MeOH-CHCl3, displaced with EtOAc)]; 4-(2-hydroxyethyl)-piperidino (HCl salt m. 239-40°); 4-propylpiperidino (m. 150-1°; HCl salt m. 246-7°); and 4-n-heptanoylpiperazino (HCl salt m. 155-62°). A mixture of 10 g. 2-diethylamino-5,7-dimethoxy-4(3H)-quinazolone-HCl 50 ml. POCl3 is refluxed 2 hrs. and evaporated to give II.HCl (Z1 = Et2N, Z2 = Cl), m. 175-84°; free base m. 129-31°; this is dissolved in 100 ml. THF, a solution of anhydrous NH3 in THF added, and the mixture stirred 24 hrs.

to

precipitate Ib, also prepared by heating a mixture of 0.1 mole 2,4,5-NC-(MeO)2C6H2NH2 in HCONMe2 and 0.5 mole Et2NC(:NH)NH2 12 hrs. at 150° and working up. A mixture of 10 g. 6,7-dimethoxy-(1H,3H)-quinazolininedione in 200 ml. pyridine and 30 g. P2S5 is refluxed 5 hrs. with stirring and worked up to give 6,7-dimethoxy-(1H,3H)-quinazolinedithione 0.22 mole MeI is slowly stirred into a solution of 0.1 mole of this in 220 ml. N KOH solution and 100 ml. MeOH, and the mixture heated 2 hrs. (steam bath) and cooled, to give I (Z1 = Z2 = SMe). Anhydrous NH3 (0.1 mole) in THF is added to 0.1 mole of this in 200 ml. THF, and the mixture stirred 18 hrs. at room temperature to precipitate I

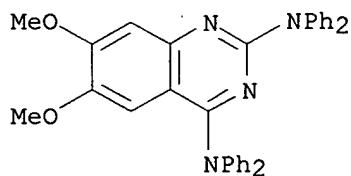
(Z1 = SMe, Z2 = NH2). A mixture of 0.1 mole of this and 0.12 mole 1-allylpiperazine in isoamyl alc. is refluxed 13 hrs. and worked up to give Id. also prepared from I (Z1 = piperazino, Z2 = NH2) by refluxing it (0.1 mole) 2 hrs. in 300 ml. MeOH containing 0.1 mole allyl bromide. 2-Furoyl chloride (0.1 mole) is stirred into 0.1 mole Ic in 300 ml. MeOH at 50°, and the mixture stirred 3 hrs. at room temperature to precipitate I [Z1 = 4-(2-furoyl)piperazino, Z2 = NH2], m. 278-80°. Biol. test data and pharmaceutical compns. are given.

IT 23680-85-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23680-85-5 HCPLUS

CN Quinazoline, 2,4-bis(diphenylamino)-6,7-dimethoxy- (8CI) (CA INDEX NAME)



L6 ANSWER 261 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1969:68419 HCAPLUS
 DOCUMENT NUMBER: 70:68419
 TITLE: Hypotensive and bronchodilatory quinolines,
 isoquinolines, and quinazolines
 INVENTOR(S): Cronin, Timothy H.; Hess, Hans J. E.
 PATENT ASSIGNEE(S): Pfizer, Chas., and Co., Inc.
 SOURCE: S. African, 114 pp.
 CODEN: SFXXAB
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| ZA 6706512 | | 19680306 | | |
| DE 1695593 | | | DE | |
| DE 1795787 | | | DE | |
| GB 1199768 | | | GB | |
| US 3517005 | | 19700623 | US | 19671026 |
| US 3594480 | | 19710720 | US | 19700312 |
| US 3702849 | | 19721114 | US | 19700317 |
| US 3812127 | | 19740521 | US 1972-259113 | 19720602 |
| PRIORITY APPLN. INFO.: | | | US | 19661031 |

GI For diagram(s), see printed CA Issue.
 AB A mixture of 5 g. 2-ethyl-4-chloro-6,7-dimethoxyquinazoline and 7.43 g. piperazine-1-carboxylic acid, iso-Bu ester in 50 ml. absolute EtOH was refluxed 1 hr. and worked up to give 79.5% 4-(2-ethyl-6,7-dimethoxyquinazolin-4-yl)-piperazine-1-carboxylic acid iso-Bu ester, m. 96-7° (hexane); HCl salt m. 218-20°. A solution of di-Et sodiomalonate in HCONMe₂ (DMF) was prepared from 11.5 g. 50% NaH-mineral oil dispersion from which the mineral oil had been removed with hexane, 32.0 g. of di-Et malonate, and 100 ml. DMF. To this was added 51.8 g. 2,4-dichloro-6,7-dimethoxy-quinazoline, and the mixture heated at 60° 40 hrs. and worked up to give 80% di-Et (2-chloro-6,7-dimethoxyquinazol-4-yl)malonate (I), m. 160.5-2.5° (EtOH). A suspension of 30 g. I in 300 ml. N NaOH was refluxed 1 hr. and filtered to give 46.5% 2-chloro-4-methyl-6,7-dimethoxyquinazoline (II), m. 183-5° (MeOH). A stainless steel pressure vessel was charged with 4.0 g. II, 40 ml. NH(Et)₂, and 40 ml. EtOH, and heated at 130° 3 hrs. and worked up to give 51% 2-diethylamino-4-methyl-6,7-dimethoxyquinazoline, m. 95-7°; HCl salt m. 220-1°. The following III (R = R₁ = MeO and R₂ = H) were prepared (R₃, R₄, m.p., and m.p. HCl salt given): H, Me, 206.8° (EtOH), 264-5°; H, Et, 223-4° (MeOH), 261-2°; H, Pr, 207-8° (EtOAc), 246-8°; H, iso-Pr, 248-50° (EtOH), 250° (decomposition); H, cyclopropyl, 237-9° (EtOAc), 253.5-4.0° (decomposition); H, Ph, 236-8°, 259-60°; H, PhCH₂, 230-1° (EtOH), 250°; H, 2-phenylethyl, 190-1° (H₂O), 239-41°; Et, Et, 112-14°, 224°; Pr, Pr, 147-8° (MeOH-H₂O), 207° (decomposition); Me, Me, 158-60°, -; and H, H, 205-7° (H₂O), 275°. Also prepared were the following III (R = R₁ = MeO, R₃ = R₄ = H) (R₂, m.p., and m.p. HCl salt given): Et, 238-9° (EtOH), 278-80°; CF₃, 284-6° (MeOH), 258-9° (decomposition); Et, -, 262-3° (decomposition); Pr, 224-6° (MeOH), 258-60° (decomposition); iso-Pr, 217-18°, 255-7°; tert-Bu, -, 272-3° (decomposition); Ph, 203-4° (MeOH), 258-60° (decomposition); PhCH₂, -, -; and PhEt, -, 270-1° (decomposition). Also prepared were the following III, (R, R₁, R₂, R₃, R₄, m.p., and m.p. HCl salt

given); CH₂:CHO, CH₂:CHO, H, H, H, 234-6° (EtOH-Et₂O), 278-81°; H, MeO, H, H, H, 270-1° (MeOH), 255-6°; and iso-Pr, iso-Pr, H, H, H, 147-8°, 250-1°. Also prepared were the following IV (R = R₁ = MeO), R₂ = H) (R₃, m.p., and m.p. HCl salt given): H, 150-1° (EtOAc), 299-30°; iso-BuCO, 125-6° (C₆H₆-hexane), -; Me, 159-60° (CH₂Cl₂-isoPr₂O), 300-1° (decomposition); CH₂:CHCH₂, 128-30° (isoPr₂O), 239-42° (decomposition); Ph, 152.5-60° (MeOH-H₂O), 221-3° (decomposition); HOCH₂CH₂, 155.8° (EtOAc), 230-3.5° (decomposition); 6,7-dimethoxy-4-quinazolyl, 264-5° (CHCl₃MeOH), 253-5° (decomposition); OH, 201-2.5° (iso-PrOH), 233° (decomposition); Ac, 186° (iso-PrOH-iso-Pr₂O), 224-5° (decomposition); EtO, 150-1° (C₆H₆-hexane), 216-17°; Me²CHO, 172-3° (C₆H₆-hexane), 210-11°; BucO, 130.5-33° (EtOAc-hexane), 209-10°; Me(CH₂)₆CO, 136-8° (MeOH-H₂O), 157-8° (decomposition); Bz, 221-3° (MeOH), 183-5°; CH₂:CHCO, 127-9° (C₆H₆-hexane), 102-4°; 2-furoyl, 159-61° (C₆H₆-hexane), 222-3°; Me²CONH, 147-8.5° (C₆H₆-iso-Pr₂O), 167-8°; CF₃CO, 191-2° (CH₂Cl₂-iso-Pr₂O), 225-6°; CC₁₃CO, 84-8° (DMF-H₂O), 243-4°; MeSO₂, 239-40° (CHCl₃-MeOH), 256° (decomposition); PhSO₂, 186-7° (C₆H₆), 236-7° (decomposition). Also prepared were 4-(6,7-dimethoxyquinazolin-4-yl)homopiperazine-1-carboxylic acid, m. 146.5-48° (EtOAc) [iso-Bu ester m. 109-12° [(iso-Pr)₂O-hexane]]; and the following IV (R = R₁ = MeO, R₂ = H, R₃ = O₂CR₄) (R₄, m.p., and m.p. HCl salt given): Et, 145-7° (C₆H₆-hexane), 215-16°; Pr, 131-3° (MeOH-H₂O), 229° (decomposition); iso-Pr, -, -; Bu, 129-30° (MeOH-H₂O), 199-200°; iso-Bu, 151-2° (MeOH), 217°; pentyl, 153-4° (MeOH), 212-12.5° (decomposition); hexyl, 143.5-45° (MeOH-H₂O), 187-7.5°; tetrahydrofurfuryl, 139-40° (C₆H₆-hexane), -; Ph, 154-5° (Me²CO), 231°; benzyl, 132-3.5° (MeOH-H₂O), 198-9°; Me²CCl₁CH₂, 158-9° (Me²CO-H₂O), -; Me²C(OH)CH₂, 199-200° (CHCl₃-EtAc), -; 2-methyl-2-propenyl, -, 210-13°; and 2-dimethylaminoethyl, 100-4° (EtOAc-hexane), 230-2°. Also prepared were 2-amino-6,7-diisopropoxyquinazoline, m. 147.5-8.5° (HCl salt m. 250-1°); 2-amino-4-methyl-6,7-dimethoxyquinazoline, m. 218-20° [HCl salt m. 282-3° (decomposition)]; and 2-dimethylamino-4-methyl-6,7-dimethoxyquinazoline, m. 131-3° (HCl salt m. 258°). Also prepared were the following 2-(4-substituted-1-piperazinyl)-4-methyl-6,7-dimethoxyquinazoline (substituent, m.p., and m.p. HCl salt given): CO₂Et, 153-5°, 247°; and CO₂Ph, 201-3°, 237.5-40.0°. Also prepared were the following IV (R = R₁ = MeO, R₃ = CO₂Bu-iso (R₂, m.p., and m.p. HCl salt given): Me, 131-2° (MeOH-H₂O), 228° (decomposition); CF₃, 132-3° (EtOH), 169-71°; Pr, 100-2° (hexane), 202-4°; iso-Pr, 102-4° (hexane), 198-9.5°; tert Bu, 89-91° (hexane), 180-1.5°; Ph, 164-6° (MeOH), 227-8° (decomposition); PhCH₂, 62-4° (CH₂Cl₂-hexane), 198-9°; Ph-CH₂CH₂, 100-1°, (C₆H₆-hexane), 190-1°; and H, -, 217° (decomposition). Also prepared were esters of 4-(6,7-dimethoxyquinoline-4-yl)piperazine-1-carboxylic acid (alc. group of ester and m.p. given): iso-Bu, 172-3° (EtOH); and CH₂C(OH)Me₂, 172-3° (EtOAc). Also prepared are the following 1-amino-6,7-dimethoxy-isoquinolines (amino group, m.p., and m.p. HCl salt given): iso-PrNH, 138-40° (MeOH), 200-4°; Me₂N, 72-5°, 148-51°; and Et₂N, 137-8.5° (Me²CO-H₂O), 189-91°. Also prepared were the following 1-(4-substituted-1-piperazinyl)-6,7-dimethoxyiso-quinolines (4-substituent, m.p., and m.p. HCl salt given): Me, 163-6° (EtOAc), 220-5°; Ph, 138-41° (MeOH), 222-8°; Ac, 137-8° (CH₂Cl₂-iso-Pr₂O), 157-8° (decomposition); and COEt, 146-7°.

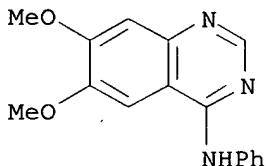
(CH₂Cl₂-iso-Pr₂O), 135-7° (decomposition). Also prepared were esters of 4-(6,7-dimethoxyisoquinolin-1-yl)piperazine-1-carboxylic acid (alc. group of ester, m.p., and m.p. HCl salt given): CH₂CH₂Cl, 137.5-38° (MeOH-H₂O), 105-6° (decomposition); CHMe₂, 155-6° (MeOH), 102-4° (decomposition); CH₂CH₂Me, 137-8° (MeOH), 120-3° (decomposition); (CH₂)₂N₂Et₂, 103-4°, (iso-Pr₂O), 78-91°; (CH₂)₂NH₂, 134-7° (EtOAc-hexane), 173-5° (decomposition); (CH₂)₂O₂Me, 119-20° (EtOAc-hexane), 103-5° (decomposition); iso-Bu, 130-2° (MeOH), -; Me₂C(OH)CH₂, 133-4° (EtOAc-hexane), -; and Me₂NCH₂CH₂, 115° (CH₂Cl₂-iso-Pr₂O), -. All title compds. exhibited bronchodilator activity, while III and the 2-aminoquinoxaline derivs. were better hypotensives. Extensive test data were given.

IT 21561-09-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 21561-09-1 HCPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 262 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1968:459169 HCPLUS

DOCUMENT NUMBER: 69:59169

TITLE: 4H-3,1-Benzoxazin-4-ones. VII. Water elimination reactions of N-(2-ureidobenzoyl)anthranilic acids

AUTHOR(S): Doleschall, G.; Lempert, K.

CORPORATE SOURCE: Tech. Univ. Budapest, Budapest, Hung.

SOURCE: Tetrahedron (1968), 24(16), 5529-45

CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal

LANGUAGE: German

GI For diagram(s), see printed CA Issue.

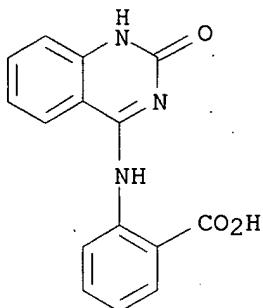
AB Dehydration of N-unsubstituted-N-(2-ureidobenzoyl)anthranilic acids (I) and (II) furnishes derivs. III and IV, resp., of 4H-3,1-benzoxazin-4-one which may subsequently be isomerized into quinazolin-2-ones (V) and (VI), resp. V may be further dehydrated to yield the quinazolino[4.3-b]quinazoline-6,8-dione (VIII). Dehydration of the N-methyl-N-(2-ureidobenzoyl)anthranilic acids (VIII) and (IX) yields spiranes X and XI, resp., XI being a stable product, while X becomes partly isomerized into XII and partly dehydrated under rearrangement into XIII. 20 references.

IT 19589-43-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

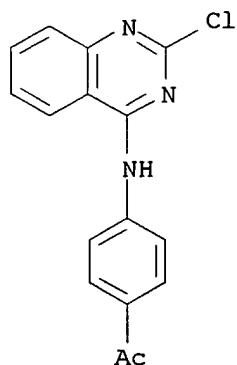
RN 19589-43-6 HCPLUS

CN Anthranilic acid, N-(1,2-dihydro-2-oxo-4-quinazolinyl)-, monohydrochloride (8CI) (CA INDEX NAME)

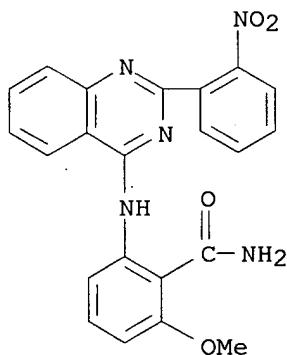


● HCl

L6 ANSWER 263 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1968:427405 HCPLUS
 DOCUMENT NUMBER: 69:27405
 TITLE: Drugs acting on the central nervous system. Syntheses of substituted quinazolinones and quinazolines and triazepino- and triazocinoquinazolinones
 AUTHOR(S): Gupta, C. M.; Bhaduri, A. P.; Khanna, N. M.
 CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, India
 SOURCE: Journal of Medicinal Chemistry (1968), 11(2), 392-5
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB 2,3-Disubstituted 4-quinazolinones, 2,4-disubstituted quinazolines, and 5H-2,3-disubstituted triazepino[1,4,5][2,1-b]-quinazolin-11-ones (I) (R = 2-furyl, Ph, Me, and p-MeOC₆H₄) are prepared and tested for toxicity and anticonvulsant activity in mice. Of the 48 compds. prepared and tested, only 2-ethylthio-4-quinazolone and 2,4-bis(dibenzylamino)quinazoline gave protection against maximum electroshock, 3 other compds. showed slight activity, and the remainder were inactive.
 IT 19062-68-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 19062-68-1 HCPLUS
 CN Ethanone, 1-[4-[(2-chloro-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 264 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1968:49551 HCPLUS
 DOCUMENT NUMBER: 68:49551
 TITLE: Cyclic amidines. XXI. Tricycloquinazoline-14C and hydroxytricycloquinazolines
 AUTHOR(S): Dean, Harvey G.; Grout, R. J.; Partridge, M. W.; Vipond, Hilton J.
 CORPORATE SOURCE: Univ. Nottingham, Nottingham, UK
 SOURCE: Journal of the Chemical Society [Section] C: Organic (1968), (2), 142-4
 CODEN: JSOOAX; ISSN: 0022-4952
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB The four isomeric hydroxytricycloquinazolines were synthesized. Hydroxyl radical oxidation of tricycloquinazoline (I) was shown to yield the 2- and 3-hydroxy derivs. Tricycloquinazoline-14C was prepared in three steps from Na14CN.
 IT 17330-46-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 17330-46-0 HCPLUS
 CN o-Anisamide, 6-[(2-(o-nitrophenyl)-4-quinazolinyl]amino]- (8CI) (CA INDEX NAME)



L6 ANSWER 265 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1965:93275 HCPLUS
 DOCUMENT NUMBER: 62:93275
 ORIGINAL REFERENCE NO.: 62:16737d-g
 TITLE: Biochemical and morphologic properties of a new lactating mammary tumor line in the rat
 AUTHOR(S): Hilf, Russell; Michel, Inge; Bell, Carlton; Freeman, James J.; Borman, Aleck
 CORPORATE SOURCE: Squibb Inst. of Med. Res., New Brunswick, NJ
 SOURCE: Cancer Research (1965), 25, 286-99
 CODEN: CNREA8; ISSN: 0008-5472
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A new transplantable mammary adenocarcinoma of the Fischer rat was studied, which arose spontaneously from the R3230AB, a fast growing, lactating tumor. The new subline, R3230AC, is autonomous, responsive, and is composed primarily of epithelial cell elements. A copious lactational

state is achieved in response to estrogen treatment and lactation is accompanied by a decrease in tumor growth rate. Androgen treatment will also decrease tumor growth rate. Biochem. studies showed that 2- to 3-fold increase in glucose-6-phosphate dehydrogenase and TPN-malic enzyme activities accompanied the estrogen-induced lactational response. Androgen treatment depressed the activities of these dehydrogenase enzymes below control levels. Isocitric dehydrogenase activity was not significantly altered. No significant anaerobic glucose utilization in vitro was obtained by R3230AC tumor, nor did treatment with estrogen alter the utilization of glucose substrate, but in vitro malic acid substrate utilization was demonstrated and estrogen treatment increased malic acid utilization. The new tumor was compared to mammary glands of the same animals. Estrogen treatment markedly increased glucose-6-phosphate dehydrogenase, TPN-malic enzyme and isocitric dehydrogenase activities. Mammary glands did not utilize glucose in vitro under anaerobic conditions, but they did utilize malic acid substrate under these conditions. The data suggest that R3230AC tumor is a transplantable breast neoplasm with certain biochem. and morphologic characteristics similar to normal breast tissue.

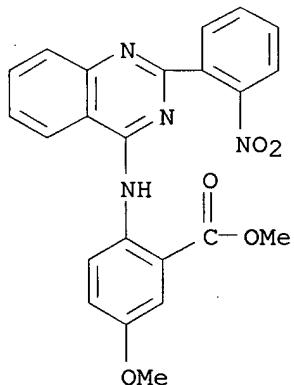
IT 2475-75-4P, m-Anisic acid, 6-[[2-(o-nitrophenyl)-4-

quinazolinyl]amino]-, methyl ester

RL: PREP (Preparation)
(preparation of)

RN 2475-75-4 HCAPLUS

CN Benzoic acid, 5-methoxy-2-[[2-(2-nitrophenyl)-4-quinazolinyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 266 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1965:93274 HCAPLUS

DOCUMENT NUMBER: 62:93274

ORIGINAL REFERENCE NO.: 62:16737b-d

TITLE: Further studies on the influence of peripheral ring substitution on the carcinogenicity of tricycloquinazoline

AUTHOR(S): Baldwin, R. W.; Cunningham, G. J.; Dean, H. G.; Partridge, M. W.; Surtees, S. J.; Vipond, H. J.

CORPORATE SOURCE: Univ. Nottingham, UK

SOURCE: Biochemical Pharmacology (1965), 14(3), 323-31
CODEN: BCPCA6; ISSN: 0006-2952

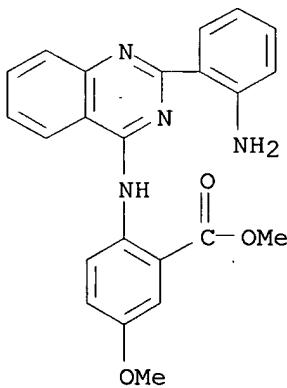
DOCUMENT TYPE: Journal

LANGUAGE: English

AB 3-Ethyl-, 3-tert-butyl-, 3-methoxy-, and 2-fluoro derivs. of tricycloquinazoline (TCQ) were unequivocally synthesized. Detns. of their

epidermal carcinogenic activities and further studies on 2-methyl-TCQ were carried out. The inactivity of 2-methyl-TCQ, both as a carcinogen and as an initiator, was confirmed, whereas 2-fluoro-TCQ was found to be active in both respects. Substitution in the 2-position of TCQ is therefore not in itself sufficient to abolish activity, and, moreover, covalent bonding of the 2-position to a receptor is not involved in TCQ carcinogenesis. Results with 3-methoxy-TCQ indicated that this substituent does not have a specific structural effect on activity. Decreases in the skin carcinoma incidence observed with 3-ethyl and 3-tert-butyl-TCQ as compared with 3-methyl-TCQ afford further support for the hypothesis that activity in TCQ and its derivs. is controlled by stereochem. factors related to the coplanar area of the mol. Comparative reassessment of the activities of all known TCQ derivs. and analogs implies a highly specific orientation of the carcinogen at the tissue receptor.

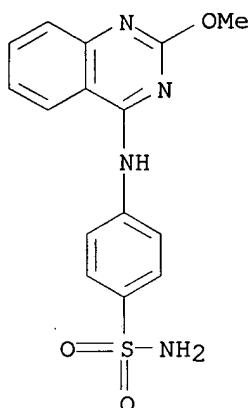
- IT 2475-72-1, Anthranilic acid, N-[2-(o-aminophenyl)-4-quinazolinyl]-5-methoxy-, methyl ester
 RL: PREP (Preparation)
 (acetyl derivative)
- RN 2475-72-1 HCAPLUS
- CN Benzoic acid, 2-[(2-(2-aminophenyl)-4-quinazolinyl)amino]-5-methoxy-, methyl ester (9CI) (CA INDEX NAME)



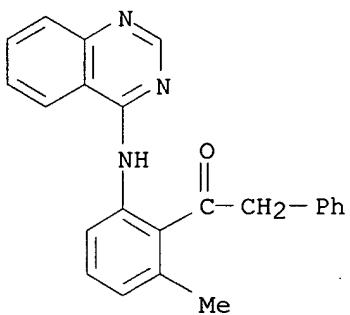
- L6 ANSWER 267 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1965:29705 HCAPLUS
 DOCUMENT NUMBER: 62:29705
 ORIGINAL REFERENCE NO.: 62:5278d-f
 TITLE: Sulfanilamidoquinazolines
 AUTHOR(S): Martin, Tellis A.; Wheeler, Allan G.; Majewski, Robert F.; Corrigan, John R.
 CORPORATE SOURCE: Mead Johnson Res. Center, Evansville, IN
 SOURCE: Journal of Medicinal Chemistry (1964), 7(6), 812-14
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 62:29705
 GI For diagram(s), see printed CA Issue.
 AB cf. Brit. 920,019, CA 59. 3935a. 2-Methoxy-4-sulfanilamidoquinazoline (I) was prepared in 40.6% from p-H2NC6H4SO2NHNa (II) and 2,4-dimethoxyquinazoline (IIa). Gas chromatographic analysis of the distillate of the reaction mixture showed substantially more than 1 mole MeOH and suggested replacement of the less reactive 2-MeO group by the solvent alc. The formation of 2-(2-methoxyethoxy)-4-sulfanilamidoquinazoline (III) was confirmed by its isolation from the

process mother liquors. III was identical with the product formed from II and 2,4-bis(2-methoxyethoxy)quinazoline, prepared by alcoholysis of IIa with MeOCH₂CH₂OH. From this latter reaction 2-methoxyquinazolin-4(3H)-one and N4-(2-methoxy-4-quinazolyl)sulfanilamide were also isolated. IIa and PhSO₂-NHNa yielded 27% N-(2-methoxy-4-quinazolyl)benzenesulfonamide. A similar reaction with IIa and PhSO₂NMeNa gave only 2-methoxyquinazolin-4(3H)-one. The antibacterial activity of III was found to be inferior to that of I.

- IT 50-87-3P, Sulfanilamide, N4-(2-methoxy-4-quinazoliny)-
 RL: PREP (Preparation)
 (preparation of)
 RN 50-87-3 HCPLUS
 CN Benzenesulfonamide, 4-[(2-methoxy-4-quinazoliny)amino]- (9CI) (CA INDEX NAME)



- L6 ANSWER 268 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1965:3107 HCPLUS
 DOCUMENT NUMBER: 62:3107
 ORIGINAL REFERENCE NO.: 62:561g-h
 TITLE: Cyclic Amidines. XIX. Derivatives of triazabenzonaphthanthracene
 AUTHOR(S): Partridge, M. W.; Slorach, S. A.; Vipond, H. J.
 SOURCE: Journal of the Chemical Society (1964), (Oct.), 3673-8
 CODEN: JCSOA9; ISSN: 0368-1769
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Both 7-benzylidene-7H-5,6a, 12-triazabenz[a]anthracene and o-quinazolin-4-ylaminophenyl benzyl ketone are cyclized with sodium aluminum chloride to give 5,10,14c-triazabeno[a]naphth[1,2,3-de]anthracene, the structure of which follows from its spectroscopic similarity to its unequivocally synthesized 14-Me derivative (I). 10,15,15d-Triazabeno[qr]naphtho[1,2,3,4-def] chrysene results similarly from 2-o-benzamidophenylperimidine. The significance of the loss of carcinogenic activity in I in tricycloquinazoline carcinogenesis is discussed.
 IT 982-55-8P, Acetophenone, 2'-methyl-2-phenyl-6'-(4-quinazolinylamino)-
 RL: PREP (Preparation)
 (preparation of)
 RN 982-55-8 HCPLUS
 CN Acetophenone, 2'-methyl-2-phenyl-6'-(4-quinazolinylamino)- (7CI, 8CI) (CA INDEX NAME)



L6 ANSWER 269 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1965:3106 HCPLUS

DOCUMENT NUMBER: 62:3106

ORIGINAL REFERENCE NO.: 62:561f-g

TITLE: Cyclic Amidines. XVIII. The synthesis of tricycloquinazolines by cyclodehydrogenation

AUTHOR(S): Partridge, M. W.; Slorach, S. A.; Vipond, H. J.

SOURCE: Journal of the Chemical Society (1964), (Oct.), 3670-3

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

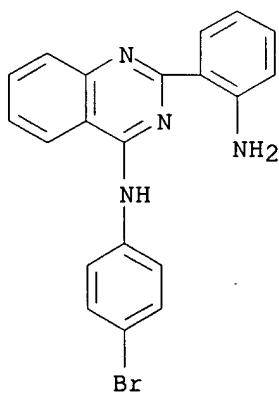
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Cyclization of 2-o-aminophenyl-4-arylaminoquinazolines with HC(OEt)₃ yields 7-aryliminotriazabenz[a]anthracenes (I) which, on cyclodehydrogenation, afford tricycloquinazolines, e.g. II.IT 855-89-0P, Quinazoline, 2-(o-aminophenyl)-4-(p-bromoanilino)-
RL: PREP (Preparation)

(preparation of)

RN 855-89-0 HCPLUS

CN Quinazoline, 2-(o-aminophenyl)-4-(p-bromoanilino)- (7CI, 8CI) (CA INDEX
NAME)

L6 ANSWER 270 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:428562 HCPLUS

DOCUMENT NUMBER: 59:28562

ORIGINAL REFERENCE NO.: 59:5170e-h,5171a-e

TITLE: Cyclic amidines. XVI. Tetraazanaphtho[1,2,3-

[fg]naphthacenes

AUTHOR(S): Parfitt, R. T.; Partridge, M. W.; Vipond, H. J.

CORPORATE SOURCE: Univ. Nottingham, Nottingham, UK

SOURCE: Journal of the Chemical Society (1963) 3062-6

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 59:28562

GI For diagram(s), see printed CA Issue.

AB cf. CA 57, 12490c. Some title compds., isomeric with tricycloquinazoline (I), were synthesized for examination of their carcinogenic activity.

9,10,15,15b-tetraazanaphtho[1,2,3-fg]naphthacene(II) is a weak epidermal carcinogen, while I is intermediate in activity between

1,2;5,6-dibenzanthracene and 3,4-benzopyrene. This contrast provides further evidence of the importance of the stereochem. fit in I

carcinogenesis. The 4a,9,10,15-isomer (III) of II is too insol. in

appropriate solvents for biol. testing. 2-Anilino-4-chloroquinazoline (4 g.) and 2.4 g. o-H₂NC₆H₄CO₂Me shaken 0.5 hr. in 50 cc. dry Me₂CO gave

2-anilino-4-(o-methoxycarbonylanilino)quinazoline-HCl (IV.HCl), m.

360-4° (EtOH); IV (from IV.HCl with alc. NH₃) m. 210-12°

(aqueous AcOH). IV heated 1 hr. at 210° and then extracted with BuOH yielded 6-anilino-7H-5,6a,12-triazabenz[a]anthracen-7-one (V), m.

190-2°. 4-Hydroxy-2-[o-(3-phenylureido)phenyl]quinazoline (VI)

(0.5 g.) in 15 cc. POCl₃ kept 12 hrs. or refluxed 1 hr. and poured onto 200 g. crushed ice yielded 74% V. 2-(o-Aminophenyl)-4-hydroxyquinazoline (VII) (5 g.) in 300 cc. dry C₆H₆ refluxed 1 hr. with 3 g. PhNCO yielded 6.1 g. VI, m. 304-6° (aqueous HCO₂H). VI fused 15 min. at

220-30° with NaOH gave 71% 2,4-dihydroxyquinazoline, m.

349-55°. VII (5 g.) in 400 cc. dry C₆H₆ and 10 g. cyclohexyl isocyanate refluxed 6 hrs. yielded 98% 2-[o(3-cyclohexylureido)] analog of VI, m. 242-4° (HCO₂H). V (1 g.) added at about 100° to a melt of 0.4 g. NaCl and 2 g. AlCl₃, heated 1 hr. at 320°, cooled, powdered, extracted with H₂O at 65°, and the extract treated with 50 cc. saturated aqueous NaNO₃ yielded II.HNO₃, dark red prisms, m. 216-18°

(precipitated

from H₂O with HNO₃). II.HNO₃ in H₂O treated with Et₃N and extracted with CHCl₃ gave II, dark green needles, m. 296-8° (CHCl₃), which

sublimed at 265-70°/0.1 mm. gave prisms, m. 296-8°. II

digested 2 days with N HCl-AcOH gave II.HCl, dark red needles, m.

328-30°; II picrate, green, m. 259-60° (AcOH). II with

H₃PO₄ in Et₂O yielded during 10 days a deliquescent phosphate, dark red needles, m. 154-6°. II (0.4 g.) in 25 cc. AcOH refluxed 15 min.with 5 cc. 30% aqueous H₂O₂ and basified with NH₄OH yielded 0.17 g. N-oxide of II, pale yellow prisms, m. 276-7° (aqueous HCONMe₂). VI (0.5 g.) and 0.6 g. NaCl-AlCl₃ heated 1 hr. at 320° gave II, isolated as 25 mg.II.HNO₃. VIII (R = OH) (IX) (1.3 g.), 0.52 g. PhNH₂, and 2 g. NaCl-AcCl₃ heated 1 hr. at 320° yielded 0.12 g. II. (o-H₂NC₆H₄)CO (1.06 g.)

and 1 g. 2,4-dichloroquinazoline in 20 cc. AcOH refluxed (0.5 hr. gave II, isolated as 0.75 g. II.HCl. II refluxed 8 hrs. with 4N HCl, 12 hrs. with

11N HCl, 5 hrs. with 5N NaOH, 5 hrs. with 10N NaOH, 24 hrs. with 2N HNO₃, 4 hrs. with 1.5N CrO₃, and 24 hrs. with 2N alkaline KMnO₄ showed 100, 42, 96, 24, 14, 41, and 20% recovery, resp. V (1 g.) in 6 cc. PhNO₂ and 0.45 g.POCl₃ refluxed 15 hrs., basified with NH₃, steam-distd, to remove the PhNO₂, and the tarry residue chromatographed on Al₂O₃ yielded 75 mg. I, m.317-19°. VI (0.5 g.) in 20 cc. 100% H₃PO₄ heated 6 hrs. at223° and poured into H₂O gave 15 mg. I. 2,4-Dianilinoquinazoline-HCl (20 g.) refluxed 4 hrs. with 50 g. KOH in 250 cc. (CH₂OH)₂, cooled, diluted with H₂O, acidified, and the precipitate extracted with EtOH gave from

the extract

9.5 g. 2-anilino-4-hydroxyquinazoline, m. 260-2° (AcOH), which was also obtained in 61% yield by hydrolysis with alc. KOH; Ac derivative m.

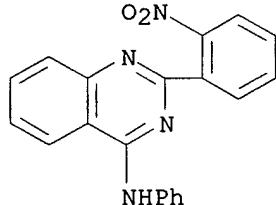
201-3°. 4-Ethoxy-2-(o-carbethoxyanilino)quinazoline (X) (0.5 g.) and 5 cc. PhNH₂ heated 6 hrs. at 180° and diluted with 5 cc. Me₂CO yielded 0.29 g. 5-anilino-12H-6,7,12a-triazabenz[a]anthracen-12-one (XI), yellow prisms, m. 298-300° (EtOCH₂CH₂OH); the mother liquor deposited 0.07 g. 4-OH analog of X, m. 210-12°, resolidifying and remelting at 290-6°. 11,12-Dihydro-11,12-dioxo-5H-5,6,11a-triazanaphthacene (XII) (2 g.) in 50 cc. POC₁₃ heated 6 hrs. at 120-40°, poured onto crushed ice, and extracted with CHCl₃ yielded 0.44 g. 6,12-dihydro-5,12dioxo-5H-6,7,12a-triaza[a]anthracene, m. 254-6°, and 1.4 g. unchanged XII. 4-Chloro-2-(o-nitrophenyl)quinazoline (XIII) (0.5 g.) and 5 g. MeNH₂.AcOH heated 1 hr. at 180°, extracted with H₂O, the insol, residue dissolved in EtOH, and basified gave 0.46 g. 4-methylamino-2-(o-nitrophenyl)quinazoline (XIV), m. 169-71° (aqueous EtOH); picrate m. 279-81°. XIII (2.9 g.), 0.83 g. PhNH₂, and 0.5 cc HCl in 150 cc. Me₂CO refluxed 0.5 hr. and cooled gave 3.1 g. 4-anilino-HCl analog of XIV, m. 192-5° (decomposition) (MeOH); free base m. 177-8° (decomposition) (BuOH). 5,6-Diazanaphthacene-11,12-diol (2 g.), 8 g. PC₁₅, and 12 cc. POC₁₃ heated 3 hrs. at 120-40°, kept 12 hrs., filtered rapidly, the filter residue mixed with 5 g. 2-aminopyridine, kept molten 0.5 hr., cooled, and extracted with H₂O left 0.17 g. III, yellow prisms, m. 370-2° (AcOH and sublimed). III with 2N aqueous-alc. H₂SO₄ gave the sulfate, yellow needles, m. 326-30° (decomposition). 11-Chloro-5,6-diazanaphthacen-12-ol (0.55 g.), 0.5 g. Cu powder, and 5 g. 2-aminopyridine refluxed 4 hrs. yielded 0.11 g. III. The ultraviolet absorption maximum of XI, the 5-piperidino analog of XI, and IX are recorded.

IT 94688-16-1P, Quinazoline, 4-anilino-2-(o-nitrophenyl)-

RL: PREP (Preparation)
(preparation of)

RN 94688-16-1 HCPLUS

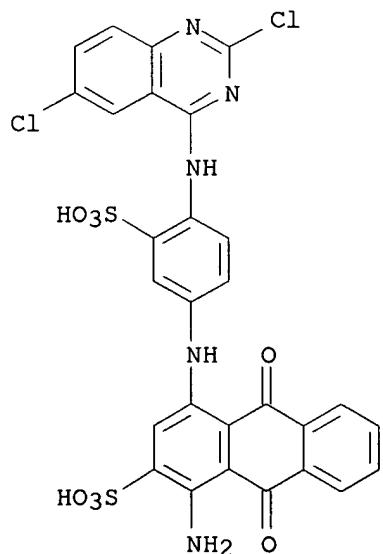
CN Quinazoline, 4-anilino-2-(o-nitrophenyl)- (7CI) (CA INDEX NAME)



L6 ANSWER 271 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1963:422238 HCPLUS
 DOCUMENT NUMBER: 59:22238
 ORIGINAL REFERENCE NO.: 59:4075a-d
 TITLE: Reactive dyes containing a chloroquinoxaline group
 INVENTOR(S): Jirou, Marcel; Brouard, Claude; Bouvet, Pierre
 PATENT ASSIGNEE(S): Compagnie Francaise des Matieres Colorantes
 SOURCE: 15 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|----------|-----------------|----------|
| FR 1308044 | ----- | 19621102 | FR | 19610922 |
| BE 621643 | ----- | | BE | |

PRIORITY APPLN. INFO.: FR 19610922
 AB Azo, phthalocyanine, and anthraquinone dyes containing a 2-chloro, 2,4- or 2,6-dichloroquin-azoline group and suitable for dyeing cotton and wool were prepared. Thus, 1,8,3,6-H2N(HO)C10H4(SO3H)2 (I) 17 was dissolved in H2O 100 with 30% NaOH, NaOAc 14 and AcOH were added to give pH 6.5-7, 6-nitro-2,4-dichloroquinazoline 14 and EtOH 20 parts were added, the mixture heated to 50-5°, cooled, filtered, and dried at 40° in vacuo to yield a yellow dye, fixed on cotton by an alkaline after-treatment at 100-50°. 6-Amino-2,4-dichloroquinazoline 5.35 was diazotized, coupled with 1,8,3,6-AcNH(HO)C10H4(SO3H)2 10 in H2O 100 and NaHCO3 8.4 parts, and salted to give a red dye. I 17 dissolved in H2O 200 with NaOH, 40% AcOH added to give pH 7, 2,4,6-trichloroquin-azoline (II) 14 and EtOH 40 parts added, the mixture heated to 60-5°, and cooled to yield 1-[(2,6-dichloro-4-quinazolinyl)-amino]-8-naphthol-3,6-disulfonic acid, which dissolved in H2O 300 with NaHCO3 and coupled neutral with diazotized 2-HO3-SC6H4NH2 8.65 parts to yield a red dye. 1,3,6-(H2N)2C6H3SO3H 18.8 dissolved in alkaline H2O 200, NaOAc 30 and 40% AcOH added to pH 6.7-7, II 28 and EtOH 40 parts added, heated to 60-5°, cooled, filtered, and the condensation product 20 dissolved in H2O 500, diazotized and coupled neutral with 1-(2,5-dichloro-4-sulfophenyl)-3-methyl-5-pyrazolone 16.2 in H2O 150 parts, and filtered gave a greenish yellow dye for printing cotton. 4,8,2-(HO3S)2C10H5N:NC6H3(NH2)Me-4,2 (III) 20 dissolved in alkaline 20 300, NaOAc 15 added, condensed with II 14 parts at 60-5°, and cooled gave a reddish yellow dye for wool. Similarly, 1-(3-aminophenyl)-3-methyl-4-(2,5-disulfophenylazo)-5-pyrazolone 22.6 and II 14 parts gave a yellow dye; the Cu complex of 2,5,7,6-H2N(HO)(HO3S)C10H4N:NC6H3(OH)SO3H-2,5 25 and II 14 parts gave a red dye; 1-amino-4-(4-amino-3-sulfoanilino)-2-anthraquinonesulfonic acid 24.5 and II 14 parts gave a blue dye; III 20 and 2,4-dichloroquinazoline-6-sulfonyl chloride 15 parts, and the SO2Cl group hydrolyzed, gave a reddish yellow dye.
 IT 96216-24-9P, 2-Anthracenesulfonic acid, 1-amino-4-[4-[(2,6-dichloro-4-quinazolinyl)amino]-3-sulfoanilino]-9,10-dihydro-9,10-dioxo-
 RL: PREP (Preparation)
 (preparation of)
 RN 96216-24-9 HCPLUS
 CN 2-Anthracenesulfonic acid, 1-amino-4-[4-[(2,6-dichloro-4-quinazolinyl)amino]-3-sulfoanilino]-9,10-dihydro-9,10-dioxo- (7CI) (CA INDEX NAME)



L6 ANSWER 272 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1963:53881 HCAPLUS
 DOCUMENT NUMBER: 58:53881
 ORIGINAL REFERENCE NO.: 58:9267a-d, 9268a-d
 TITLE: Photographic layers for the silver decolorization process
 PATENT ASSIGNEE(S): CIBA Ltd.
 SOURCE: 30 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| BE 611898 | | 19620622 | BE | |
| CH 404398 | | | CH | |
| DE 1138318 | | | DE | |
| GB 940286 | | | GB | |
| US 3211555 | | 19651012 | US 1961-160938 | 19611220 |
| PRIORITY APPLN. INFO.: | | | CH | 19601223 |

GI For diagram(s), see printed CA Issue.

AB Photog. layers for the Ag decolorization process are obtained by incorporating into the Ag halide emulsion a quinazoline or a 4-quinazolone containing an arylazo group. 4-Hydroxyquinazoline (87.6 parts) and 125 parts PC15 in 600 vols. o-C₆H₄Cl₂ heated 20 min. at 185°, the mixture concentrated by the removal of 150 vols. liquid, cooled, treated with

108.6 parts 2,5-(EtO)₂C₂H₃NH₂. heated 2 h. at 150°, the solvent steam distilled, the residue treated with Na₂CO₃ and filtered gave 4-(2,5-diethoxyanilino)quinazoline (I), grayish green powder, m. 104-6° (50% EtOH). I (82 parts) in 500 vols. AcOH treated during 15 min. with 35.7 vols. HNO₃ (d15 1:505) and 50 vols. AcOH, heated 0.5 h. at 35-40° cooled overnight, and filtered yielded 4-(4-nitro-2,5-diethoxyanilino)quinazoline (II), yellow powder, m. 209-12° (AcOH). II (114 parts) in 900 vols. HCONMe₂ hydrogenated at 20-50° over Raney Ni, filtered, diluted with cold H₂O, and refiltered gave the 4-NH₂ analog (III) of II, green powder, m. 133-6° (C₆H₆). III (6.9 parts) and 7 vols. HCl (d. 1.195) in 100 parts H₂O diazotized at 0-5°, treated during 20 min. with the p-ethoxyanilide 6.2 of 2,3-HOC₁₀H₅CO₂H (IV) and Na₂CO₃ 10 in HCONMe₂ 100 parts, stirred 2 h. at room temperature, and filtered gave 8.65 parts V, blue needles (o-C₆H₄Cl₂). V 0.64, saponin 0.32, and H₂O 20 were ground in a ball mill to a particle size of less than 0.5 μ, diluted with H₂O 80, mixed with 6.25% gelatin solution 320, a portion 100 of the solution mixed with a red-sensitized AgBr-gelatin emulsion 200 parts, the mixture coated on glass plates and dried, exposed, developed with a MeOH-hydroquinone developer, fixed, bleached in a bath containing 30-100 vols. 37% HCl/1000 vols., 40-120 parts KBr, 30-50 parts CS(NH₂)₂, and 0.001-0.1 part aminohydroxyphenazine and then in a bath containing 100 parts NaCl, 100 parts CuSO₄·5H₂O, and 50 vols. 37% HCl, and fixed in the usual manner gave a blue, pos. image of the original Ag image. 4-Chloroquinazoline solution from 87.6 parts 4-hydroxyquinazoline heated 2.5 h. with 91.2 parts 2,5-Me-(O₂N)C₆H₃NH₂ at 140°, cooled, and filtered, and the resulting beige powder, m. 210-15°, hydrogenated over Raney Ni gave 4-(5-amino-2-methylanilino)quinazoline (VI), m. 174-8°, beige powder. VI (5 parts) diazotized and coupled with the p-tolylamide of IV yielded a red powder which gives, in the usual manner by the Ag decolorization process, a red, pos. image. Similar dyes were prepared from

the following 4-substituted quinazolines (4-substituent and m.p. given):
 4,2-H2N(MeO)C6H3NH, 161-3°; p-H2NC6H4NH, 213-15°;
 m-H2NC6H4NH, 242-5°; 4,2,5-H2N(MeO)2C6H2NH, 98-100°;
 4,5,2-H2N(Me)(MeO)C6H2NH (VII), 181-4°; 4,5,2-H2N(Cl)(MeO)C6H2NH,
 210-12°; 4,2,5-isomer of VII, 192-4°; and from
 4-hydroxy-7-aminoquinazoline (VIII), 293-5°. 6-Amino-4-
 hydroxyquinazoline (m. 295-300°) treated with p-O2NC6H4COCl, and
 the resulting product hydrogenated gave 6-(p-aminobenzamido)-4-
 hydroxyquinazoline (IX), m. 309-11°. The azo dye 1, obtained by
 coupling diazotized IX with 3-methyl-5-pyrazolone, Na
 diisobutylnaphthalenesulfonate 1, and H2O 20 parts ground in a ball mill
 to a particle size of <0.5 μ, the ground mixture added to sufficient
 gelatin solution to obtain a colored solution containing 6% dry gelatin, 5%
 dye, and

5% dispersing agent, and a portion 150 added to AgBr emulsion 150 parts
 and then coated on a film support gave material useful for the production of a
 colored image by the Ag decolorization process. Similar dyes, usable in
 this invention, were obtained from 2,4-dihydroxy-7-aminoquinazoline, m.
 320°; 4-hydroxy-2-(p-aminophenyl)quinazoline, m. 277-9°;
 2-methyl-3-(p-aminophenyl)-4-quinazolone, m. 220-3°;
 4-(p-aminoanilino)-6-aminoquinazoline, m. .apprx.260°;
 2-methyl-3-(4'-amino-4-biphenyl)-4-quinazolone, m. 284-8°.

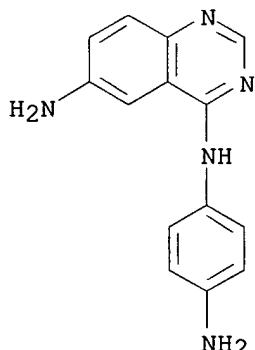
IT 92193-49-2, Quinazoline, 6-amino-4-(p-aminoanilino)-

RL: PREP (Preparation)

(azo compds. from, for color photog.)

RN 92193-49-2 HCPLUS

CN Quinazoline, 6-amino-4-(p-aminoanilino)- (7CI) (CA INDEX NAME)



L6 ANSWER 273 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:3286 HCPLUS

DOCUMENT NUMBER: 58:3286

ORIGINAL REFERENCE NO.: 58:521d-f

TITLE: Polyzazanaphthalenes. VII. Some derivatives of
quinazoline and 1,3,5-triazanaphthalene

AUTHOR(S): Oakes, V.; Rydon, H. N.; Undheim, K.

CORPORATE SOURCE: Univ. Exeter, UK

SOURCE: Journal of the Chemical Society (1962) 4678-85
CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 58:3286

GI For diagram(s), see printed CA Issue.

AB 2,4-Diamino-6-methylquinazoline was synthesized and converted, by
side-chain bromination of its dibenzoyl derivative, condensation with ethyl

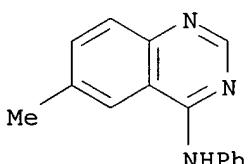
p-aminobenzoate, and removal of the benzoyl and ester groups, into the pteroic acid analog (I). A similar procedure has led to the successful synthesis of pteroic acid analogs derived from 2,4-diamino- and 2-amino-4-hydroxy-1,3,5-triazanaphthalene. The expected preferential reactivity of the 4-chlorine atom in 2,4-dichloro-6-methylquinazoline is exhibited in its reactions with ammonia, hydrazine, and benzylamine, but not in that with aniline.

IT 92554-57-9P, Quinazoline, 4-anilino-6-methyl-

RL: PREP (Preparation)
(preparation of)

RN 92554-57-9 HCPLUS

CN 4-Quinazolinamine, 6-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 274 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:463343 HCPLUS

DOCUMENT NUMBER: 57:63343

ORIGINAL REFERENCE NO.: 57:12670e-i,12671a

TITLE: Asymmetric azo compounds

PATENT ASSIGNEE(S): Farbenfabriken Bayer A.-G.

SOURCE: 5 pp.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|----------|-----------------|----------|
| GB 887262 | ----- | 19620117 | GB 1960-19825 | 19600603 |
| DE 1150469 | ----- | | DE | |

PRIORITY APPLN. INFO.: DE 19590618

AB Asym. azo compounds were prepared by treating syn-diazo sulfonates with diazo compds. of the naphthalene or benzene series between 0 and 80° in weakly acid or alkaline medium. anti-Sulfonates could also be used by irradiation to the corresponding syn-sulfonates. Some of the new compds. can be used as textile dyes or as starting materials for polyazo dyes. The diazo solution 100 ml. of 2-ClC₆H₄NH₂ (I) 4.6 g. was introduced with rapid stirring into an ice-cold solution of crystalline Na₂SO₃ 8 g. and anhydrous Na₂CO₃ 13.5 g. in H₂O 52 ml., NaCl 20 g. added, and the precipitate

was

filtered and washed with an ice-cold saturated NaCl solution to give an orange-yellow syn-sulfonate. The moist paste in a cold solution of anhydrous NaOAc 8.4 g. in H₂O 100 ml. was treated with 90 ml. solution of diazotized 1,4-H₂N(HO₃S)C₁₀H₆ (II) (3.23 g.), the precipitate stirred overnight, filtered, taken up in H₂O 300 ml. and slowly heated to 80°; after cooling and salting 1,4-(2-ClC₆H₄N:N)(NaO₃S)C₁₀H₆ was obtained as pale brown crystals, yellow in H₂O, red-violet in concentrated H₂SO₄. The reaction can be carried out in the presence or absence of light. The anti-sulfonate yielded only traces of the reaction product in the absence of light, yielding larger quantities on exposure to light. Similarly, other azo compds. were prepared (diazo sulfonate component, diazonium component, color in H₂O, color in concentrated H₂SO₄ given): 4-H₂NC₆H₄N:NC₆H₄SO₃H-4 (III), 2,8-H₂NC₁₀H₆SO₃H (IV)

(or IV, III), orange, red-violet; IV, 2-C10H, NH2 (V), yellow; reddish blue; 2,5,7-H2N(PhSO2O)C10H5SO3H, V (product saponified), yellow, blue (orange with alkali); 6,2,4,8-O2N(H2N)C10H4(SO3H)2 (VI), V, yellow, orange; 4-H2NC6H4OH, 4-AcNHCl5H4NH2 (VII), -, -; IV, VII (product saponified), -, -; VI, VII (product saponified), -, -; I, 3,4-HO2CCO NH(HO3S)C6H3NH2 (product saponified), yellow, -; VI, 4-MeOC6H4NH2, yellow, orange-yellow; 4-amino-4'-(p-anisylazo)-2,2'-stilbenedisulfonic acid, IV, yellow, violet; 4-H2NC6H4SO3H (VIII), 1-C10H7NH2, yellow, reddish blue; dehydrothiotoluidinedisulfonic acid, IV, yellow, orange-red; VIII, 2,6,4,8-H2N(AcNH)C10H4(SO3H)2 (product saponified), yellow, -.

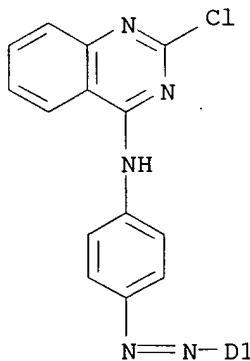
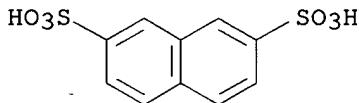
IT 102111-29-5P, 2,7-Naphthalenedisulfonic acid, acetamido[[p-[(2-chloro-4-quinazolinyl)amino]phenyl]azo]hydroxy-

RL: PREP (Preparation)
(preparation of)

RN 102111-29-5 HCAPLUS

CN 2,7-Naphthalenedisulfonic acid, acetamido[[p-[(2-chloro-4-quinazolinyl)amino]phenyl]azo]hydroxy- (7CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

D1-NH-Ac

D1-OH

L6 ANSWER 275 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:463342 HCAPLUS
 DOCUMENT NUMBER: 57:63342
 ORIGINAL REFERENCE NO.: 57:12670a-e
 TITLE: Azo dyes
 INVENTOR(S): Barker, Peter W.; Hunter, James S.; Waite, Frederick A.
 PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.
 SOURCE: 11 pp.

DOCUMENT TYPE:

Patent

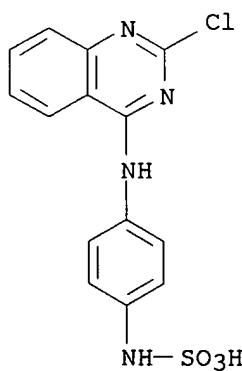
LANGUAGE:

Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------------------|----------|-----------------|----------|
| GB 892323 | | 19620328 | GB 1959-27833 | 19590814 |
| PRIORITY APPLN. INFO.: | | | GB | 19590814 |
| GI For diagram(s), see printed CA Issue. | | | | |
| AB Sulfamic acid derivs. of the general formula I are diazotized and treated with coupling components to give yellow to red dyes for cotton. Thus, 18.8 parts 4-H ₂ NC ₆ H ₄ NHSO ₃ H (II) is condensed with 18.6 parts cyanuric chloride (III) at pH 7. A solution of HN(CH ₂ CH ₂ OH) ₂ 10.5 in H ₂ O 50 is added, the mixture is stirred for 2 hrs. at 35-40°, then for 20 hrs. at 45-50° at pH 7 to give I, X = N(CH ₂ CH ₂ OH) ₂ , R = Y = Z = H (IV). Similarly, I are prepared (compound number, X, Y, Z, R given): V, Cl, H, H, H; VI, MeO, H, H, H; VII, Cl, Cl, H, H; VIII, PhNH, H, H, H; IX, benzothiazol-2-yl-thio, H, H, H; X, Cl, MeO, Me, H; XI, Cl, H, H, Me. An isomer (XII) of V is prepared from III and 3-H ₂ NC ₆ H ₄ NHSO ₃ H. Analogs of I (XIII, XIV, and XV) are prepared from II and 2,4,6-trichloropyrimidine, 2,4-dichloro-5-cyanopyrimidine, and 2,4-dichloroquinazoline, resp. Diazotized IV coupled with p-MeC ₆ H ₄ OH (XVI) gave a 37.3% yield of yellow dye [82.2% yield when IV was diazotized in the presence of poly(glycerol ricinoleate)]. Similarly, other dyes were prepared (diazo component, coupling component, % yield, and shade given): XIII, XVI, 66.7, yellow; V, 1-C ₁₀ H ₇ NHCH ₂ CH ₂ OH, 47, red; V, m-C ₆ H ₄ (OH) ₂ , 50.3, orange; V, 2,6-ClCH ₂ COC ₁₀ H ₆ OH, 43.3, red; VI, XVI, 58, yellow; XII, 1,8,3,6-AcNH(HO)C ₁₀ H ₄ (SO ₃ H) ₂ (XVII), 73.4, red; VII, 1-phenyl-3-methyl-5-pyrazolone, (XVIII), 70.5, yellow; XIV, XVI, 32.7, yellow; VIII, 1,2,6-H ₂ N(MeO)C ₁₀ H ₅ SO ₃ H, 59.3, red; IX, 4'-SO ₃ H derivative of XVIII, 63.2, yellow; XV, XVII, 44.5, red; X, PhNHCOCH ₂ Ac, 60.8, greenish yellow; XI, XVI, 54.9, yellow; IV, m-MeC ₆ H ₄ N(CH ₂ CH ₂ OH) ₂ , 62.9, orange; IV, 2,5,7,1-H ₂ N(HO)(HO ₃ S)C ₁₀ H ₄ N: NC ₆ H ₄ SO ₃ H-2, 63.3, brown. | | | | |
| IT 93309-34-3P, Sulfamic acid, [p-[(2-chloro-4-quinazolinyl)amino]phenyl]- | | | | |
| RL: PREP (Preparation) | | | | |
| | (preparation of) | | | |
| RN 93309-34-3 HCPLUS | | | | |
| CN Sulfamic acid, [p-[(2-chloro-4-quinazolinyl)amino]phenyl]- (7CI) (CA INDEX NAME) | | | | |



DOCUMENT NUMBER: 57:62771
 ORIGINAL REFERENCE NO.: 57:12490c-i,12491a-i,12492a-d
 TITLE: Cyclic amidines. XV. Derivatives of tricycloquinazoline
 AUTHOR(S): Partridge, M. W.; Vipond, H. J.; Waite, J. A.
 CORPORATE SOURCE: Univ. Nottingham, UK
 SOURCE: Journal of the Chemical Society (1962) 2549-56
 CODEN: JCSOA9; ISSN: 0368-1769
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.
 AB cf. CA 55, 9422a. Unsym. substituted tricycloquinazolines, required for examination of the relevance of the symmetry of tricycloquinazoline to its carcinogenic activity, were synthesized by a number of routes. 5-Fluoroisatin (15 g.) in 150 ml. 2.5N NaOH treated dropwise with 27 ml. 30% H₂O₂, heated 15 min. at 80-90°, filtered through C, and the filtrate treated with concentrated HCl gave 7 g. 5,2-F(H₂N)C₅H₃-CO₂H, m. 182-3° (xylene). 2-NCC₅H₄NH₂ (I) (11.8 g.) in 40 ml. dry C₆H₆ and 20 ml. pyridine shaken 1 hr. with 20 g. 2-O₂NC₆H₄COCl (II) in 70 ml. C₆H₆, the C₆H₆ distilled, and the residue treated with 300 ml. H₂O gave 16.4 g. 4,2 R(NC)C₆H₃NHCOC₆H₄NO₂-2 (III) (R = H), m. 205-6° (EtOH). Similarly were prepared 61% III (R = Me), m. 185-6° (EtOH), and 58% III (R = Br), m. 190-7° (AcOH or BuOH). II (65 g.) in 200 ml. C₆H₆ added during 10 min. to 49 g. 5,2-Me(H₂N)C₆H₃CO₂H in 500 ml. 0.8N NaOH with stirring, the mixture stirred 30 min., and the aqueous layer adjusted to pH 4 with AcOH gave 69 g. x,2-R(2-O₂-NC₆H₄CONH)C₆H₃CO₂H (IV) (R = 5-Me), m. 229.5-31.0° (BuOH). The following IV were prepared similarly (R, % yield, m.p., recrystn. solvent given): 3-Me, 209-10°, EtOH; 5-Br, 75, 251-2 BuOH; 5-F, 70, 252-3°, EtOH. IV (R = 5-Me) (68 g.) boiled 1 hr. with 200 ml. Ac₂O gave 58 g. V (R = Me, R' = H), m. 186.5-8.0° (AcOH). The following V were prepared similarly (R, R', % yield, m.p., recrystn. solvent given): H, Me, 86, 186-7 AcOH; Br, H, 86, 145-6°, EtOH; F, H, 92, 170-1°, AcOH. Method A. III (R = H) (5 g.) in 15 ml. dioxane and 100 ml. 20% aqueous NaOH refluxed 1 hr. with 60 ml. 30% H₂O₂, the solution treated with 25 ml. 30% H₂O₂, refluxed 30 min., diluted with 500 ml. H₂O, neutralized with AcOH, and made alkaline with aqueous NH₃ gave 4.35 g. VI (R = R' = H) (VIa), m. 227-8° (PhMe). Method B. V (R = R' = H) (30 g.) and 150 g. urea heated 30 min. at 180-90° and poured into 1.25 l. H₂O with stirring gave 26 g. Via, m. 227-9° (BuOH). By the foregoing methods were prepared the following VI (R, R', method, % yield, m.p., recrystn. solvent given): Me, H, A, 88, 271-3° BuOH; Me, H, B, 92, 271-3°, BuOH; H, Me, B, 74, 286-8°, AcOH; Br, H, A, 90, 279-80°, AcOH; Br, H, B, 79, 279-80 AcOH; F, H, B, 68, 248-9°, MeOCH₂CH₂OH (VII). VIa (2.7 g.) in 20 ml. 2N NaOH treated gradually with 10.5 g. Na₂S₂O₄ at 80° while maintaining the pH above 9 by further addns. of 2N NaOH, after 30 min. the solution cooled, and neutralized with AcOH gave 1.4 g. VIII (R = R' = H) (VIIIa) m. 239-41°. Raney Ni added portion-wise to 2.7 g. VIa and 4 ml. 80% N₂H₄.H₂O (IX) in 80 ml. EtOH at 60-5° until effervescence subsided and the mixture filtered deposited 1.56 g. VIIIa, m. 240-1°; 2-(2-nitrobenzoyl) derivative (X) (formed with II) m. 272-3°. Reduction of the VI with Raney Ni and IX in EtOH or BuOH gave the following VIII (R, R', % yield, m.p., recrystn. solvent given): Me, H (XI), 76, 223-4° [HCl salt m. 279-81° (2N HCl)], iso-PrOH; H, Me (XII), 78, 259-60°, BuOH; Br, H, (XIII), 67, 264-5°, BuOH; F, H (XIV), 68, 266-7°, EtOH. VIIIa (1 g.) refluxed 90 min. in 25 ml. pyridine with 1.4 g. 2-phthalimidobenzoyl chloride, diluted with H₂O, and the alkali-sol, fraction worked up gave 1.1 g. 2-(2-phthalimidobenzoyl) derivative (XV) of VIIIa, m. 316-18° (PhMe). Reduction of X with Raney Ni and IX in EtOH gave 24% 2-(2-amino-benzoyl)

derivative (XVI) of VIIia, m. 314-16° (BuOH). XV (0.3 g.) in 20 ml. VII refluxed 2 hrs. with 0.5 ml. 80% IX and the solution neutralized with HCl gave 0.11 g. XVI. XI (0.75 g.) and 0.6 g. II in 16 ml. dry C6H6 and 25 ml. pyridine refluxed 90 min., the C6H6 removed, and the residual solution diluted with H2O gave 0.87 g. corresponding amide (XVII), m. 272-3° (BuOH); the mother liquors deposited 0.045 g. compound, probably the secondary amide, m. 24950°. Reduction of XVII with Raney Ni and IX gave 58% 2-(2-aminobenzoyl) derivative (XVIII) of XI, m. 317-20° (BuOH); Ac derivative m. 295-7° (BuOH). Catalytic reduction of XVII in AcOH over PtO2 gave 52% XVIII. From VIIia and 2-(4-MeC6H4SO2NH)C6H4COCl was prepared 61% corresponding amide (XIX), m. 266-7° (BuOH). VIa (2.7 g.), 0.73 g. HCONMe2, and 15 ml. SOC12 boiled 75 min., cooled, and poured onto 100 g. crushed ice with stirring gave 2.7 g. 4-chloro-2-(2-nitrophenyl)quinazoline (XX), m. 179-81° (anhydrous Me2CO). VIa (40 g.) and 160 ml. POCl3 heated 2.5 hrs. at 140°, filtered hot, and the filtrate kept at 0° gave 20.6 g. XX, m. 179-81°; from the mother liquor was obtained 9.3 g. XX, m. 178-80°. XX (2.85 g.), 1.51 g. 2-H2NC6H4CO2Me, and 0.2 ml. concentrated HCl in 150 ml. Me2CO refluxed 1 hr. gave 4 g. XXI (R = CO2Me, R' = R'' = H) (XXII) HCl salt, m. 232-3° (MeOH); XXII (obtained from XXII·HCl in MeOH with aqueous NH3) m. 187-8° (AcOH). The following XXI were prepared similarly (R, R', R'', % yield, m.p., m.p. of HCl salt given): CO2H, H, H, 70, 309-11°, 253-5°; CN, H, H, 74, 186-7°, -; CO2Me, Me, H, 74, 196-7°, 173-5° (decomposition) (containing EtOH of crystallization); CO2Me, H, Me, 69, 214-15°, 217-19° (decomposition); CN, H, Me, 83, 197-9°, 192-3° (decomposition) (containing AcOH of crystallization); CN, H, OMe, 76, 197-8°, 161-2°. XXII (2.2 g.) in 150 ml. AcOH shaken with H and 0.01 g. PtO2, filtered, the filtrate evaporated, the residue extracted with acid, and the extract basified gave 1.3 g. XXIII (R = CO2Me, R' = R'' = H) (XXIV), m. 192-3° (BuOH); HCl salt m. 176-8 (2N HCl); Ac derivative m. 212-13° (AcOH). Reduction of XXII with Raney Ni and IX in BuOH as described above gave 76% XXIV, m. 191-3°. By the latter reductive procedure were prepared the following XXIII (R, R', R'', % yield, m.p., recrystn. solvent given): CO2Me, Me, H (XXV), 75, 152-3°, MeOH; CO2Me, H, Me (XXVI), 90, 182-3°, BuOH; CN, H, Me (XXVII), 59, 195-6° (decomposition), PhMe; CN, H, OMe (XXVIII), 60, 201-3° (decomposition), BuOH. I (3 g.) and 8 g. Me anthranilate ptoluenesulfonate heated 40 min. at 210° and the product extracted with hot acid and alkali gave 1.02 g. tricycloquinazo-line (XXIX), m. 317-20°, having the characteristic bands between 245 and 455 μ neutralization of the acid and alkaline exts. gave 0.4 g. 5-amino-11-hydroxyphenhomazine, isomeric with VIIia, m. 213-15° (MeOH) [di-Ac derivative m. 238-9° (AcOH)]. VIIia (0.6 g.), 0.3 g. I, and 0.1 g. 4-MeC6H4SO3H heated 45 min. at 210°, the powdered product washed with warm 2N HCl and 2N NaOH, and extracted with C6H6 gave 0.49 g. XXIX, m. 318-20°. The following derivs. of XXIX were prepared similarly by the latter method (reactants, derivative of XXIX formed, % yield, m.p. given): XII and I, 1-Me (XXX), 31, 292-4°; VIIia and 5,2-Me(NC)C6H3NH2, 2-Me (XXXI), 31, 278-9 (XXVII) heated 1 hr. at 210° underwent cyclization and gave 30% XXXI, m. 278-80°; VIIia and 4,2-Me(NC)C6H3NH2 (XXXII) (obtained in 47% yield by pyrolysis of 5-methylisatin 3-oxime), 3-Me (XXXIII), 31, 266-7 XI and I, 3-Me, 33, 266-7°; VIIia and 3,2-Me(NC)C6H3NH2, 4-Me (XXXIV), 20, 246-8°; VIIia and 4,2-Br(NC)C6H3NH2 (XXXV), 3-Br, 34, 290-1°; XIII and I, 3-Br, 35, 290-1°; VIIia and 4,2-F(NC)C6H3NH2 (XXXVI) [b15 130 m. 94-5° (H2O)], 3-F, 30, 322-3°; XI and XXXII, 3,8-Me2, 42, 273-5°; XIII and XXXV, 3,8-Br2, 18, 325-6°; XIV and XXXVI, 3,8-F2, 29, 336-8°. XVI (0.1 g) and 0.4 g. P2O5 in 15 ml. xylene boiled 90 min. and subsequently

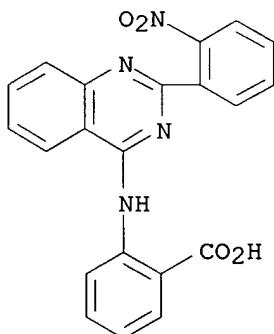
treated with H₂O gave 20 mg. XXIX, m. 317-20°. XVIII and XIX treated similarly gave 23% XXXIII, m. 264-6°, and 17% XXIX, m. 318-20°, resp. XXII treated similarly gave 23% XXXIII, m. 264-6°, and 17% XXIX, m. 318-20°, resp. XXII treated similarly gave (from the acid-soluble fraction) 30% recovered XXII and (as the acid-insol. fraction) 14% XXIX, m. 319-20°. XXII (0.5 g.) and 25 g. 100% H₃PO₄ heated 3 hrs. at 160° (optimum time and temperature) and poured into 70 ml. H₂O gave 0.34 g. XXIX, m. 319-20° (PhMe). Similar treatment of XXVI and XXV gave 80% XXXI, m. 278-9°, and 70% XXXIII, m. 266-7 resp. XXXII.4-MeC₆H₄SO₃H heated 45 min. at 210° gave 11% 3,8,13-trimethyltricycloquinazoline, m. 388-90° (xylene). XXVIII (1 g.) heated 2 hrs. at 255° gave 0.73 g. 2-methoxytricycloquinazoline (XXXVII), m. 250-1° (PhMe). XXXVII demethylated by boiling 1 hr. with aqueous HBr gave 92% 2-hydroxytricycloquinazoline, m. 367-9 (aqueous pyridine). From preliminary biol. observations, the most significant indication was that XXXI was almost noncarcinogenic, whereas XXX, XXXIII, and XXXIV were carcinogenic. Spectral data for the tricycloquinazolines were recorded.

IT 94873-30-0P, Anthranilic acid, N-[2-(o-nitrophenyl)-4-quinazolinyl]-

RL: PREP (Preparation)
(preparation of)

RN 94873-30-0 HCPLUS

CN Anthranilic acid, N-[2-(o-nitrophenyl)-4-quinazolinyl]- (7CI) (CA INDEX NAME)



L6 ANSWER 277 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:436355 HCPLUS

DOCUMENT NUMBER: 57:36355

ORIGINAL REFERENCE NO.: 57:7269g-i,7270a

TITLE: Reaction of anthranilonitrile and N-methylantranilonitrile with phenyl isocyanate and phenyl isothiocyanate

AUTHOR(S): Taylor, Edward C.; Ravindranathan, R. V.

CORPORATE SOURCE: Princeton Univ., Princeton, NJ

SOURCE: Journal of Organic Chemistry (1962), 27, 2622-7

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:36355

AB The condensation of anthranilonitrile with phenyl isothiocyanate is known to give N-phenyl-N'-(o-cyanophenyl)thiourea. This compound upon short boiling in methanol is converted quant. to 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline, which in turn, upon refluxing in aqueous dimethylformamide, rearranges to 2-thio-4-anilino-1,2-dihydroquinazoline.

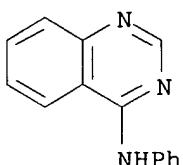
This is formed directly quant. from anthranilonitrile and phenyl isothiocyanate under more vigorous conditions. Structures of all products are rigorously established and the mechanism of the rearrangement is discussed. Anthranilonitrile condenses similarly with phenyl isocyanate to give either N-phenyl-N'-(o-cyanophenyl)urea, 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline, or 2-oxo-4-anilino-1,2-dihydroquinazoline, depending upon the reaction conditions. Analogous reactions of N-methylantranilonitrile with both phenyl isothiocyanate and phenyl isocyanate are discussed. 2-Methylthio-3-phenyl-4-methylimino-1,2,3,4-tetrahydroquinazoline rearranges in high yield to 2-anilino-3-methyl-4-oxo-3,4-dihydroquinazoline upon treatment with base. The mechanism of this rearrangement is discussed.

IT 34923-95-0P, Quinazoline, 4-anilino-

RL: PREP (Preparation)
(preparation of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 278 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1961:112218 HCPLUS

DOCUMENT NUMBER: 55:112218

ORIGINAL REFERENCE NO.: 55:21152b-e

TITLE: Quinazolines

INVENTOR(S): Meerwein, Hans

PATENT ASSIGNEE(S): Schering Akt.-Ges.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|------|
| | DE 1074047 | | 19600128 | DE | |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | N:CR.N:CR'.C:C.CH:CH.CH:CH (I) [R is alkyl or aryl, R' is the radical derived from R'CN (II)], were prepared by heating II, RCR''':NR''' (III) (R'' is Cl or alkoxy, R''' is aryl, unsubstituted on at least one ortho position), and a Friedel-Crafts catalyst (IV) (method A) or RCONHR''', SOC12, or PC15, II, and IV (method B) or II and the nitrilium compds. from III (R'' = Cl) and IV (method C) or III and the addition compds. from II and IV (method D), in suitable solvents at 90-160°. Thus, (method B) heating 19.7 g. BzNPh in 50 ml. II (R' = Ph) (V) with 13 g. SOC12 and 13.3 g. AlCl3 1 hr. at 150° (HCl and SO2 evolved), treating the cooled mixture with NaOH, and distilling excess V with steam gave 85.7% I (R = R' = Ph) (VI), m. 119-20° (EtOH), also prepared (method A) from V, III (R = R''' = Ph, R'' = Cl, OMe and OEt resp.), and AlCl3 in 96%, 86%, and 93% yield. The addition compound from V with ZnCl2 was heated in o-Cl2C6H4 (VII) 10 min. at 100° with III (R = R''' = Ph, R'' = Cl) to give approx. 100% VI (method D). The following I were prepared (R, R', method, R'', R''', solvent, IV, m.p., crystallization solvent, and % yield given): Ph, | | | | |

Me,

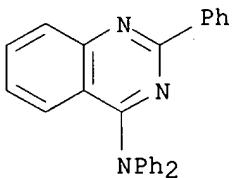
C, Cl, Ph, MeCN, TiCl₄, 90°, EtOH, 85; Ph, Br, C, Cl, Ph, PhNO₂, SnCl₄, 129°, AcOEt, 70.8; CC₁₃, Ph, A, Cl, Ph, V, AlCl₃, 129°, EtOH, 78.8; Ph, CHPh₂, A, Cl, Ph, PhNO₂, AlCl₃, 132°, EtOH, 94; Me, Ph, A, OEt, Ph, V, AlCl₃, 47° (b1 191°), -, 72; Ph, SMe, C, Cl, Ph, PhNO₂, SnCl₄, 94°, EtOH, 98; Ph, Ph₂N, A, Cl, Ph, VII, SnCl₄, 156°, EtOH, -; Ph, PhN:C(Ph)NH, C, Cl, Ph, VII, SnCl₄, 196.5-7.0, Am₂O, 88. I (R = Ph, R' = Ph₂N) hexachlorostannate, m. 276-9° (PhCN).

IT 103051-13-4P, Quinazoline, 4-diphenylamino-2-phenyl-

RL: PREP (Preparation)
(preparation of)

RN 103051-13-4 HCPLUS

CN 4-Quinazolinamine, N,N,2-triphenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 279 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1961:27922 HCPLUS

DOCUMENT NUMBER: 55:27922

ORIGINAL REFERENCE NO.: 55:5516c-e

TITLE: 2-Deoxy-D-ribose. IV. A direct synthesis of
2'-deoxyadenosine and its anomer through
2-deoxy-D-ribose derivatives

AUTHOR(S): Ness, Robert K.; Fletcher, Hewitt G., Jr.

CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD

SOURCE: Journal of the American Chemical Society (1960), 82,
3434-6

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 55:27922

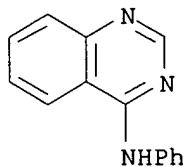
AB cf. CA 54, 6744f; 55, Number 6. 2-Deoxy-D-ribose was converted to 2-deoxy-D-ribose diisobutyl dithioacetal, which by mono-p-nitrobenzoylation was converted to a 5-O-p-nitrobenzoyl derivative. Demercaptalation of this, followed by further p-nitrobenzoylation, gave the two anomeric 2-deoxy-D-ribofuranose tri-p-nitrobenzoates (β , m. 172-3°, $[\alpha]_{D}^{20}$ 17.1° (c 0.36, CHCl₃); α , m. 165-6°, $[\alpha]_{D}^{20}$ 70.7° (c 0.33, CHCl₃)). Conversion of these esters to amorphous 2-deoxy-3,5-di-O-p-nitrobenzoyl-D-ribosyl chloride, followed by condensation with chloromercuri-6-benzamidopurine and removal of the protecting groups, led to the isolation of 2'-deoxyadenosine (10% yield), its anomer, 9-(2-deoxy- α -D-ribofuranosyl)adenine (19% yield, m. 209-11°, $[\alpha]_{D}^{2558}$ 71° (c 0.54, H₂O), λ 260 μm , and molar absorbancy 15,900 at 260 μm , and a third nucleoside, which was probably 7-(2-deoxy- α -D-ribofuranosyl)adenine. 2-Deoxy-5-O-trityl- α -D-ribose was prepared by direct tritylation of 2-deoxy-D-ribose in dry pyridine (40% yield).

IT 34923-95-0P, Quinazoline, 4-anilino-

RL: PREP (Préparation)
(preparation of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 280 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1961:27921 HCAPLUS

DOCUMENT NUMBER: 55:27921

ORIGINAL REFERENCE NO.: 55:5515h-i,5516a-c

TITLE: Reaction of 4-quinazolinecarbonitrile with nucleophilic reagents. I

AUTHOR(S): Higashino, Takeo

CORPORATE SOURCE: Coll. Pharm., Shizuoka

SOURCE: Yakugaku Zasshi (1960), 80, 1404-7

CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 55:27921

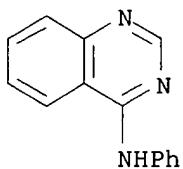
AB 4-Quinazolinecarbonitrile (I) (0.3 g.) in 3 ml. 10% KOH agitated vigorously 15 min., 1 ml. AcOH added, and the mixture left standing gave quant. 4-quinazolinone (II), m. 216-18°. I (0.2 g.) in 5 ml. 2N HCl stirred 30 min. and the solution neutralized with K₂CO₃ gave quant. II. 4-Alkoxy-6-methyl-2-pyrimidinecarbonitrile and 4-alkoxy-2-quinazolinecarbonitrile did not react with alkali. I (0.5 g.) in MeONa (0.1 g. Na and 10 ml. MeOH) heated 15 min., the MeOH removed, and the residue in H₂O extracted with C₆H₆ gave 0.3 g. 4-methoxyquinazoline (III), m. 36°. MeONa (0.1 g. Na and 6 ml. MeOH) treated with 0.4 g. PhOH, the mixture heated 10 min., 0.5 g. I added, the mixture refluxed 30 min., the solvent removed, the residue in H₂O extracted with C₆H₆, and washed with 3% KOH gave 0.2 g. III and 0.11 g. 4-phenoxyquinazoline, m. 78-9°. I (0.3 g.) in 3 ml. MeOH treated with 0.2 g. 80% N₂H₄.H₂O in 1 ml. MeOH and kept at room temperature gave quant. 4-hydrazinoquinazoline (IV), m. 188-9° (decomposition). IV (0.35 g.) in 25 ml. MeOH and 0.3 g. PhCHO refluxed 3 hrs., the MeOH removed, and the product recrystd. (C₆H₆) gave quant. 4-benzylidenehydrazinoquinazoline, m. 171-2°. I (0.5 g.) and 0.3 g. BuNH₂ reacted with heat evolution to give 0.43 g. 4-butylaminoquinazoline, m. 116-17° (petr. ether). I (0.15 g.) and 0.15 g. piperidine kept 1 hr. at room temperature, the product taken up in CHCl₃, and washed with H₂O gave 0.14 g. 4-piperidinoquinazoline; picrate m. 193-4°. I (0.5 g.) and 0.3 g. PhNH₂ heated 2 hrs. at 100° and the product washed with C₆H₆ gave 0.38 g. 4-anilinoquinazoline, m. 215-17° (MeOH).

IT 34923-95-0P, Quinazoline, 4-anilino-

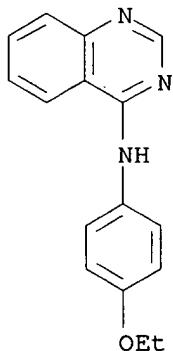
RL: PREP (Preparation)
(preparation of)

RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 281 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1960:110594 HCPLUS
 DOCUMENT NUMBER: 54:110594
 ORIGINAL REFERENCE NO.: 54:21119f-g
 TITLE: Preparation of 4-(p-carbethoxyphenylamino)quinazoline and 4-(p-ethoxyphenylamino)quinazoline
 AUTHOR(S): Biniecki, Stanislaw; Muszynski, Eugeniusz
 CORPORATE SOURCE: Akad. Med., Warsaw
 SOURCE: Acta Polon. Pharm. (1960), 17, 99-101
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB The p-CO₂Et and p-OEt derivs. of 4-phenylaminoquinazoline-HCl, m.
 253° and 235° (EtOH), resp., were prepared by treating at room
 temperature in 10 ml. EtOH 1.3 g. 4-chloroquinazoline with 1.3 g.
 p-H₂NC₆H₄CO₂Et
 or p-H₂NC₆H₄OEt.HCl, resp. The yield was 65%.
 IT 857202-28-9P, Quinazoline, 4-p-phenetidino-, hydrochloride
 RL: PREP (Preparation)
 (preparation of)
 RN 857202-28-9 HCPLUS
 CN Quinazoline, 4-p-phenetidino-, hydrochloride (6CI) (CA INDEX NAME)



● HCl

L6 ANSWER 282 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1960:110593 HCPLUS
 DOCUMENT NUMBER: 54:110593
 ORIGINAL REFERENCE NO.: 54:21119e-f
 TITLE: Preparation of different series of quinoxaline derivatives. H. Reinheckel
 SOURCE: Monatsberichte der Deutschen Akademie der Wissenschaften zu Berlin (1959), 1(No. 11), 698-9

CODEN: MDAWAH; ISSN: 0011-9814

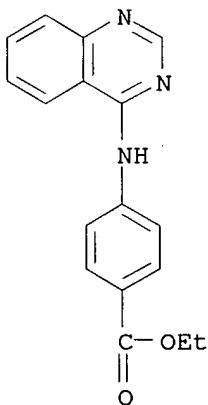
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB α -Oxo acids reacted with o-phenylenediamine in alc. HCl giving directly 2-hydroxy-3-alkylquinoxalines (I). I with POCl_3 or POBr_3 gave 2-halo-3- alkylquinoxalines (II). II underwent substitution reactions with alcoholates or amines. Hydrazine hydrate reacted quite easily with II to give stable 2-hydrazino-3-alkylquinoxalines. α -Oximino dicarboxylic acid esters reacted with o-phenylenediamine in alc. HCl to give esters of ω -(2-hydroxy-3-quinoxalyl) fatty acids. Similarly, esters of α -oximino fatty acids reacted with 1,2-diaminonaphthalene to give a mixture of both possible isomers of 2-hydroxy-3-alkylbenzoquinoxalines. Analogously, esters of α -oximino and α -oxo dicarboxylic acids gave esters of ω -(2-hydroxy-3-benzoquinoxalyl) fatty acids.

IT 109696-74-4P, Benzoic acid, p-4-quinazolinylamino-, ethyl ester hydrochloride
 RL: PREP (Preparation)
 (preparation of)

RN 109696-74-4 HCPLUS

CN Benzoic acid, p-4-quinazolinylamino-, ethyl ester, hydrochloride (6CI)
 (CA INDEX NAME)



● HCl

L6 ANSWER 283 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1957:51873 HCPLUS
 DOCUMENT NUMBER: 51:51873
 ORIGINAL REFERENCE NO.: 51:9625b-i, 9626a
 TITLE: Studies in potential amebicides. III. Synthesis of 4-substituted amino-8-hydroxy (and 8-methoxy) quinazolines and 3-substituted 8-hydroxy (and 8-methoxy)-4-quinazolones
 AUTHOR(S): Iyer, R. N.; Anand, Nitya; Dhar, M. L.
 CORPORATE SOURCE: Central Drug Research Inst., Lucknow
 SOURCE: Journal of Scientific & Industrial Research (1956), 15C, 1-7
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 50, 5676a. An attempt was made to increase the antipathogenic

activity of 8-hydroxyquinolines by adding another N atom to the hetero ring and by the inclusion of extra-annular side chains of varying electropolar character. The synthesis of 3-methoxyanthranilic acid was accomplished by preparing the imide of 3-methoxyphthalic anhydride followed by a Hofmann reaction or m-MeOC₆H₄CHO was nitrated, oxidized to the acid, and reduced catalytically to the 3-methoxyanthranilic acid. The latter, when treated with formamide gave 3-methoxyquinazolone (I), m. 298°. The 4-alkylamino-8-methoxyquinazolines were prepared by condensing I with various amines in dry benzene and refluxing 24 hrs. I was treated with 2.1 g. PCl₅ and 5 cc. POCl₃ (5 cc.) 6 hrs. at 130-40°, then 1.76 g. POCl₃ removed in vacuo, and the residue refluxed with 3 g. n-butylamine. Benzene was removed, the residue rubbed with 10% NaOH solution, washed with ether, and crystallized from aqueous alc. The following 8-methoxyquinazolines were

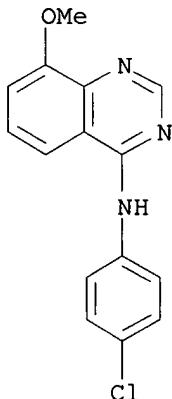
prepared similarly: 4-n-butylamino, m. 190°; 4-n-pentylamino, m. 162°; 4-p-chlorobenzylamino, m. 227°; and 4-isopentylamino, m. 178°. The n-octyl, m. 144°, n-dodecyl, m. 93°, and NHCHMe(CH₂)₃NET₂, m. 158°, derivs. were also prepared and isolated in ether and dried with KOH and recrystd. from aqueous alc. The piperidino derivative b4 227° and was extracted with CHCl₃. The 4-alkylamino-8-hydroxyquinazolines were prepared by demethylation of the previous methoxyquinazolines by two methods. 4-n-Butylamino-8-methoxyquinazoline (0.2 g.) was refluxed with 0.46 g. AlCl₃ in 25 cc. pure dry benzene 3 hrs., the residue cooled in ice, 6N H₂SO₄ then added and the sulfate decomposed with K₂CO₃. The free base m. 127° (from aqueous alc.). Alternatively, 0.5 g. methoxyquinazoline was heated with 1.2 g. pyridine-HCl at 150° 10 hrs., the mixture dissolved in water and K₂CO₃ added, the mixture extracted with an Et₂O-CHCl₃ mixture and the HO compound

extracted with 2% aqueous NaOH. The alkaline extract was adjusted to pH 6 with dilute HOAc

and precipitate filtered off. The residue m. 127° (from aqueous alc.). The following 8-hydroxyquinazolines were similarly prepared: 4-n-pentylamino, m. 112°; 4-isopentylamino, m. 112°; 4-n-hexylamino, m. 142°; 4-n-heptylamino, m. 137°; 4-n-octylamino, m. 119°; 4-n-dodecylamino, m. 78°; 4-benzylamino, m. 155°; 4-p-chlorobenzylamino, m. 220°; 4-p-methoxybenzylamino, m. 162°; and 4-piperidyl, m. 141°. 5,7-Diodo-8-hydroxyquinazoline, m. 226°, was prepared by treating 0.3 g. 8-hydroxyquinazoline with 4.5 cc. ICl. 8-Methoxy-3-methyl-4-quinazolone, m. 172°, and the 3-Et, m. 108°, 3-Pr, m. 113°, 3-iso-Pr, m. 138°, 3-Bu, m. 78°, 3-benzyl, m. 118°, derivs. were prepared by treating 1.76 g. 8-methoxy-4-quinazolone in 25 cc. MeOH and 0.6 g. KOH with the appropriate alkyl halide at 10°. The Na derivative of 8-methoxy-4-quinazolone (1.7 g. quinazolone and 0.8 g. NaOH) in 40 cc. absolute alc. was refluxed with 4.04 g. β-chloroethyl p-toluenesulfonate to give 8-methoxy-3-(β-chloroethyl)-4-quinazolone, m. 140° also prepared from 3.5 g. 8-methoxyquinazolone and ClCH₂CH₂OH with subsequent reaction with 20 cc. SOCl₂. The following derivs. were similarly prepared: 3-(β-diethylaminoethyl), b4 224°; 3-(β-di-n-butylaminoethyl), b4 232°; 3-(β-di-n-pentylaminoethyl), b4 238°; 3-(β-di-n-heptylaminoethyl), b4 248°; and 3-(β-piperidinoethyl), b9 228°. The 3-substituted 8-hydroxy-4-quinazolones were prepared by treating the quinazolone with constant-boiling HBr 10 hrs. at 140°. The following derivs. were prepared (3-substituent, m.p., and recrystg. solvent given): H, 295°, H₂O; Me, 153°, H₂O; Et, 118°, H₂O; Pr, 96°, H₂O; iso-Pr, 128°, H₂O; Bu, 87°, H₂O; PhCH₂, 160°, dilute alc.; CH₂CH₂OH, 189°, H₂O; CH₂CH₂Br, 158°, C₆H₆. Similarly prepared were di-HCl salts of 3-CH₂CH₂NR₂ analogs (R, m.p., and crystallizing solvent

given): Et, 206°, alc.-petr. ether; Bu, 183°, acetone-petr. ether (II); n-pentyl, 169°, II; n-heptyl, 152°, II; (NR2 =) piperidino, 158°, II.

IT 100865-50-7P, Quinazoline, 4-p-chloroanilino-8-methoxy-
RL: PREP (Preparation)
(preparation of)
RN 100865-50-7 HCPLUS
CN Quinazoline, 4-p-chloroanilino-8-methoxy- (6CI) (CA INDEX NAME)



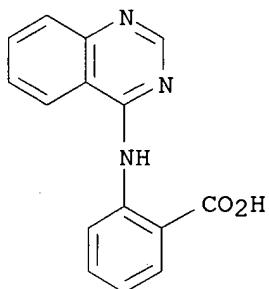
L6 ANSWER 284 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1957:34884 HCPLUS
 DOCUMENT NUMBER: 51:34884
 ORIGINAL REFERENCE NO.: 51:6647h-i,6648a-i,6649a
 TITLE: Syntheses in the quinazolone series. II. Synthesis of quino- and quinazoquinazolones
 AUTHOR(S): Stephen, T.; Stephen, Henry
 CORPORATE SOURCE: Univ. Witwatersrand, Johannesburg, S. Afr.
 SOURCE: Journal of the Chemical Society (1956) 4173-7
 CODEN: JCSOA9; ISSN: 0368-1769
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 50, 15540g. The synthesis of quinazolones was extended to the condensation of Me anthranilate (I) and of NH4 anthranilate (II) with cyclic imidoyl chlorides; i.e., compds. containing N: CCl as part of a ring structure, viz., 2-chlorolepidine (III) and its derivs. and 4-Cl (IV) and 4-chloro-2-phenylquinazoline (V). In the condensation of III and its derivs. with I, it was found that if equimolar proportions of the reactants were used the yield was 10-30% lower than if one molar excess of I was used. The condensation was carried out as follows: III or a derivative (1 equivalent) were heated with 2 equivs. I in an oil bath, and when separation of
 I.HCl was complete the mixture made alkaline, and steam distilled to remove excess
 I and any unchanged III. III (1.7 g.) and 2.7 g. I heated 10 min. at 130° gave 1.5 g. Me N-2'-lepidylantranilate (VI), m. 149° (from alc.). III (1.7 g.) and 2.7 g. I heated 15 min. at 170° yielded 5-methylquino[2,1-b]quinazol-12-one (VII), yellow needles, m. 213°; platinichloride, buff. VI was readily soluble in concentrated HCl but from refluxing HCl the HCl salt of VII separated, this on treatment with H2O and neutralization liberated free VII. An alc. solution of VI refluxed 0.5 hr. with 10% NaOH and acidified gave N-2'-lepidylantranilic acid, needles, m. 203-4°. 2-Chloro-4,6-dimethylquinoline (VIII) (1 g.) and 1.6 g. I 0.5 hr. at 140° gave 50% Me N-(4,6-dimethyl-2-

quinolyl)anthranilate (IX) and 0.4 g. recovered VIII. IX crystallized as needles, m. 162.5° (from 75% dioxane). Attempts to improve the yield gave mixts. of IX and 3,5-dimethylquino[2,1-b]quinazol-12-one (X). Refluxing the reactants several hrs. in dry dioxane gave no reaction. X obtained in 93% yield after 15 min. treatment at 170°, m. 199°. 2-Chloro-4,7-dimethylquinoline (XI) (1 g.) and 1.6 g. I 0.5 hr. at 140° gave 80% Me N-(4,7-dimethyl-2-quinolyl)anthranilate (XII), white needles, m. 172° (from 75% dioxane). Condensation at 170-90° gave an inseparable mixture of XII and the quinazolone (XIII), which was entirely converted to XIII by refluxing concentrated HCl or hydrolyzed to N-(4,7-dimethyl-2-quinolyl)anthranilic acid (XIV). Condensation of 1 g. 2-chloro-4,8-dimethylquinoline (XV) with 1.6 g. I 10 min. at 140° gave 80% Me N-(4,8-dimethylquinolyl)anthranilate, needles, m. 170°. The following analogs of VII were prepared (substituent, temperature of reaction, time in min., % yield, and m.p. given): 2-Me (XVa), 200-20°, -, 100, 194.5°; 2-MeO (XVI), 200-20°, 10, 96, 230°; 2-EtO (XVII), 200-20°, 10, 95, 193°. Analogs of XIV were prepared from the ester and(or) the quinoquinazolone by hydrolysis with NaOH in refluxing aqueous dioxane. These acids were converted to quinoquinazolones when sublimed or refluxed with Ac₂O (product, starting material, time of hydrolysis in hrs., m.p. given): 4,6-di-Me, IX, 0.5, 236°; XIV, XII and XIII, 0.5, 242°; 4-Me, 7-MeO (XVIII), XVI, 1, 218°; 4-Me, 7-EtO (XIX), XVII, 1, 188°. These acids, except XIX, were converted to quinoquinazolones. No condensation occurred between 2-chloro-6-ethoxylepidine and I below 150°, or when refluxed in solvents such as PhMe, or xylene 2-4 hrs. Condensation at 150-70° resulted in mixts. converted to XVII by refluxing with HCl, or hydrolyzed to XIX by NaOH. 2-Chloro-6-methoxylepidine (XX) (2 g.) and 2.7 g. I did not condense below 150°, but 0.5 hr. at 150-60° gave mixts. of the ester and XVI, but when refluxed with concentrated HCl gave only XVI. Condensation of XX with I 10 min. at 200-20° gave 96% XVI, canary yellow needles, m. 230° (from dioxane). XV (1 g.) and excess I heated to the b.p. gave N-(4,8-dimethyl-2-quinolyl)anthranilic acid (XXI). Thus, the ester first formed failed to undergo ring closure but dry HCl hydrolyzed the ester group. XXI crystallized as needles, m. 240° (from dioxane). Ring closure by heating above the m.p. or refluxing with Ac₂O failed. The ester in dioxane on hydrolysis with 10% NaOH gave XXI. Refluxing XXI with concentrated HCl gave the HCl salt as cream colored crystals.

IV (3 g.) left 1 hr. in Me₂CO with 5.6 g. I yielded 5.6 g. solids which on addition of NH₃ gave Me N-4'-quinazolinylanthranilate (XXII), needles, m. 211° (from dioxane); HCl salt, m. 195°. The Me₂CO filtrate and washings gave 2.5 g. unchanged I. XXII heated at its m.p. until effervescence ceased afforded quinazo[4,3-b]quinazol-8-one (XXIII), m. 197°. IV (2 g.) in 20 ml. Me₂CO treated at 0° with 2 g. II in Me₂CO gave an immediate precipitate of NH₄Cl and after 1 hr. the solid removed, and the filtrate concentrated giving N-4'-quinazolinylanthranilic acid (XXIV), m. 248° (decomposition), which gave a platinichloride. XXIV heated at 250° gave XXIII. V (2 g.) and 2.7 g. I refluxed 2 hrs. in PhMe gave Me N-(2-phenyl-4-quinazolinyl)anthranilate (XXV), needles, m. 179° (from dioxane). XXV refluxed 1 hr. with Ac₂O gave 6-phenylquinazo[4,3-b]quinazol-8-one (XXVI), m. 292°. XXV (0.5 g.) refluxed 0.5 hr. in dioxane with 10% NaOH gave N-(2-phenyl-4-quinazolinyl)anthranilic acid (XXVII), yellow needles, m. 255° (decomposition) (from aqueous dioxane). V (1.2 g.) in Me₂CO at 0° treated with 0.8 g. II in Me₂CO at 0°, left 1 hr., the filtrate evaporated, the product refluxed with H₂O to remove anthranilic acid, and treated with NH₃ gave 2-phenylquinazol-4-one (XXVIII). Acidification of the NH₃ solution gave XXVII. XXVII heated at 255-60° gave a mixture, showing that it did not readily cyclize, probably due to steric hindrance by the 2-Ph group.

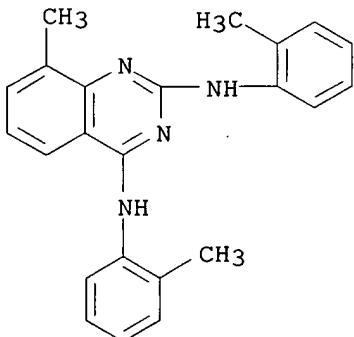
Refluxing XXVII with Ac₂O 1 hr. gave XXVI. V (0.6 g.) and 0.7 g. anthranilic acid refluxed 1 hr. in PhMe gave a compound, m. 240-5° (from aqueous dioxane). The product treated with cold NH₄OH gave an insol. portion identified as XXVIII. The NH₃ solution on acidification deposited XXVII, m. 255°.

IT 33683-28-2, Anthranilic acid, N-4-quinazolinyl-
RL: PREP (Preparation)
(and derivs.)
RN 33683-28-2 HCPLUS
CN Benzoic acid, 2-(4-quinazolinylamino)- (9CI) (CA INDEX NAME)

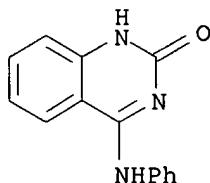


L6 ANSWER 285 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1957:34881 HCPLUS
 DOCUMENT NUMBER: 51:34881
 ORIGINAL REFERENCE NO.: 51:6646a-d
 TITLE: Synthesis of 2,4-di(arylarnino)quinazoline and its derivatives. II
 AUTHOR(S): Dymek, Wojciech; Malicki, Juliusz; Waksmundzka, Antonina
 CORPORATE SOURCE: Zaklad Chem. Org. Wydz. Mat.-Fiz.-Chem. U.M.C.S., Lublin
 SOURCE: Ann. Univ. Mariae Curie-Sklodowska, Lublin-Polonia, Sect. AA (1955), Volume Date 1953, 8, 65-70
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 49, 1731g. sym-Di-o-tolylguanidine (5 g.) and 3.7 g. o-MeC₆H₄NCS heated 3 hrs. at 220° treated with 30 ml. EtOH and 10 ml. concentrated HCl, and kept for a long period gave a crystalline precipitate, which, recrystd. from EtOH, treated with concentrated Na₂CO₃, boiled 15 min., filtered, washed with H₂O, and recrystd. from EtOH gave 2,4-di(o-toluidino)-8-methylquinazoline (I), rods, m. 138-40°; mono-HCl salt, m. 240-2°; monopicrate, m. 268-70°. I (2 g.) in 20 ml. 50% alc. KOH autoclaved 4 hrs. at 140°, and the hydrolyzate dissolved in 20 ml. H₂O, filtered, lightly acidified with HCl, and crystallized from EtOH gave 2-hydroxy-4-o-toluidino-8-methylquinazoline, m. 243°. I (2 g.) autoclaved 4 hrs. at 160° gave 2,4-dihydroxy-8-methylquinazoline, m. 283°. Di-o-tolylguanidine (2 g.) and 1.3 g. PhNCS heated 3 hrs. at 220°, treated hot with EtOH, cooled, and crystallized from EtOH yielded 2-o-toluidino-4-anilino-8-methylquinazoline (III), m. 140-2°; mono-HCl salt (IV), m. 310°. IV (2 g.) dissolved in 20 ml. 50% alc. KOH 4 hrs. autoclaved at 140°, dissolved in H₂O, filtered, acidified with HCl, and recrystd. from EtOH gave 2-hydroxy-4-anilino-8-methylquinazoline, m. 249-52°. IV (2 g.) 4 hrs. autoclaved at 160-80° gave 2,4-dihydroxy-8-methylquinazoline, m. 283°.
 IT 115209-85-3, Quinazoline, 8-methyl-2,4-di-o-toluidino-

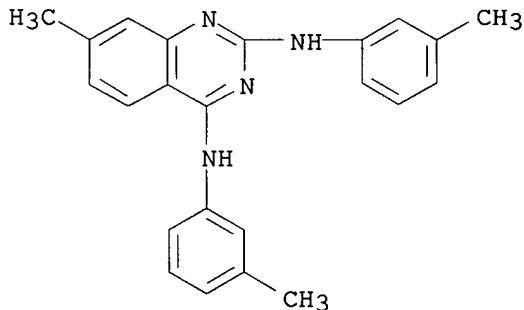
RL: PREP (Preparation)
 (and derivs.)
 RN 115209-85-3 HCPLUS
 CN Quinazoline, 8-methyl-2,4-di-o-toluidino- (6CI) (CA INDEX NAME)



L6 ANSWER 286 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1957:25579 HCPLUS
 DOCUMENT NUMBER: 51:25579
 ORIGINAL REFERENCE NO.: 51:5095d-e
 TITLE: Reactions of acetamide with aniline and phenyl isothiocyanate
 AUTHOR(S): Dymek, Wojciech; Brzozowska, Natalia; Brzozowski, Tadeusz
 CORPORATE SOURCE: Mariae Curie-Sklodowska Univ., Lublin
 SOURCE: Ann. Univ. Mariae Curie-Sklodowska, Lublin-Polonia
 Sect. AA (1956), Volume Date 1954, 9, 35-43
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB Acetamide (I), aniline (II) and PhNCS (III) are heated at 200-20° to yield 2,4,6-trianilino-1,3,5-triazine (IV); 2,4-dianilinoquinazoline (V), m. 152°, and acetanilide. V (1 g.) boiled with 10 ml. Ac2O yields 2,4-bis(acetylanilino)quinazoline, m. 148-50°. V heated under pressure with KOH at 130° for 4 hrs. yields 4-anilino-2-hydroxyquinazoline (VI), m. 252-54°; picrate, m. 262°; hydrochloride, m. 256-7°. VI with 15% KOH and Me2SO4 yields 2-methoxy-4-anilinoquinazoline, m. 198-200°. The mechanism of the reaction is postulated.
 IT 67461-77-2, 2-Quinazolinol, 4-anilino-
 RL: PREP (Preparation)
 (and derivs.)
 RN 67461-77-2 HCPLUS
 CN 2(1H)-Quinazolinone, 4-(phenylamino)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1957:25564 HCAPLUS
 DOCUMENT NUMBER: 51:25564
 ORIGINAL REFERENCE NO.: 51:5087e-g
 TITLE: Additional syntheses and transformations of compounds
 of the 2,4-diarylaminquinazoline type. III
 AUTHOR(S): Dymek, Wojciech
 CORPORATE SOURCE: Mariae Curie-Sklodowska Univ., Lublin
 SOURCE: Ann. Univ. Mariae Curie-Sklodowska, Lublin-Polonia
 Sect. AA (1956), Volume Date 1954, 9, 45-52
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB 2,4-Di(m-toluidino)-7-methyl-quinazoline (I) is prepared by heating N,
 N'-di(m-tolyl) guanidine with m-tolyl isothiocyanate at 180-200°;
 hydrochloride, m. 256-57°; phosphate, m. 252-54°; picrate,
 m. 290-91°. I with alc. KOH under pressure at 180° is
 converted to 2,4-dihydroxy-7-methylquinazoline, m. 315-17°.
 2,4-Di(p-toluidino)-6-methylquinazoline (II) is prepared by heating
 N,N'-di(p-tolyl) guanidine with p-tolyl isothiocyanate (III) at
 180-200°. II is also prepared by the condensation of acetamide with
 III at 200-20°. II hydrochloride, m. 320-21°; picrate, m.
 289°; mono-Ac derivative m. 262° (decomposition); di-Ac derivative, m.
 213-16°. II with alc. KOH under pressure at 160-80° is
 converted to 4-p-toluidino-2-hydroxy-6-methylquinazoline, m. 302°.
 IT 115209-84-2, Quinazoline, 7-methyl-2,4-di-m-toluidino-
 RL: PREP (Preparation)
 (and derivs.)
 RN 115209-84-2 HCAPLUS
 CN 2,4-Quinazolinediamine, 7-methyl-N,N'-bis(3-methylphenyl)- (9CI) (CA
 INDEX NAME)



L6 ANSWER 288 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1956:77929 HCAPLUS
 DOCUMENT NUMBER: 50:77929
 ORIGINAL REFERENCE NO.: 50:14773i,14774a-i,14775a-e
 TITLE: Nitrilium salts. II. A new quinazoline synthesis
 AUTHOR(S): Meerwein, Hans; Laasch, Peter; Mersch, Rudolf;
 Nentwig, Joachim
 CORPORATE SOURCE: Univ. Marburg, Germany
 SOURCE: Chemische Berichte (1956), 89, 224-38
 CODEN: CHBEAM; ISSN: 0009-2940
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 50:77929
 GI For diagram(s), see printed CA Issue.
 AB Warming 5.8 g. N-phenylbenzonitrilium hexachlorotitanate (I.TiCl₆) in 10
 cc. MeCN a few min. at 65-70°, making the mixture alkaline, and extracting it

with Et₂O gives 85% 2-phenyl-4-methylquinazoline (II), needles, m. 90°; similarly, heating I.SnCl₆ 10 min. with PhCN gives 96.5% 2,4-diphenylquinazoline (III), m. 119-20°. Heating 2.4 g. PhCN.ZnCl₂ and 2.1 g. benzanilide imide chloride (IV) in 20 cc. o-C₆H₄Cl₂ 10 min. at 100° and decomposing the oil formed with H₂O gives 100% III; with PhCN.SnCl₄, III.SnCl₆, yellow needles, m. 201-3°, is obtained. When 21.6 g. IV in 50 cc. PhCN is treated with 13.3 g. AlCl₃ the temperature rises to 130°; the mixture is kept a few min. at 110-20°, decomposed with 20% NaOH, filtered, and the oil steam distilled, leaving 96% III. N-phenylbenzimino Me treated similarly to IV 20 min. at 160-70° formed 86% III. Boiling 10.8 g. IV in 60 cc. MeCN a few min. with 6.5 g. SnCl₄ and decomposing the mixture with NaOH gives 62.5% II. Adding 6.7 g. AlCl₃ to 10.8 g. IV in 25 cc. EtCN and boiling the mixture a few min. gives 88% 2-phenyl-4-ethylquinazoline, m. 45° (picrate, red-yellow crystals, m. 139°). Heating 4 g. N-phenylacetimino Et ether in 30 cc. PhCN with 3.5 g. AlCl₃, 20 min. at 170-80°, steam distilling the mixture, and extracting the residue with Et₂O gives 72% 2-methyl-4-phenylquinazoline, b.p. 191°, m. 47°. Adding 6.7 g. AlCl₃ to 10.8 g. IV and 9.7 g. Ph₂CHCN in 30 cc. PhNO₂, heating the mixture a few min. at 120-30°, adding H₂O, and steam distilling the organic layer leaves 94% 2-phenyl-4-diphenylmethylquinazoline, m. 132°. Heating 2.6 g. N-phenyltrichloroacetamide chloride in 3 cc. MeCN with 3 g. SnCl₄ 10 min. at 125° gives 71% 2-trichloromethyl-4-methylquinazoline, long needles, m. 144°; with AlCl₃ the yield is 58%, with TiCl₄, 65%. Adding 5.3 g. BrCN to a cooled mixture of 11 g. IV in 20 cc. PhNO₂ and 6.5 g. SnCl₄ and 30 cc. PhNO₂ and heating the mixture in a sealed tube 10 min. at 150° gives 86.3% 2-phenyl-4-bromoquinazoline (V) hexachlorostannate, m. 214-16°; free V, shiny needles, m. 129°. Adding in 3 portions with shaking 7.3 g. MeCNS to 21.5 g. IV and 15 g. SnCl₄ in 70 cc. PhNO₂ causes a rise in the temperature to 100-20° and the separation of 98% 2-phenyl-4-methylthioquinazoline (VI) hexachlorostannate, large yellow crystals, m. 278-81°, which, decomposed with NaOH, gives VI, needles, m. 94°. Warming 13 g. trichloroacetanilide imide chloride in 40 cc. PhNO₂ with 3.6 g. MeCNS and 6.5 g. SnCl₄ 10 min. at 150° and decomposing the filtered precipitate with NaOH gives 90% 2-trichloromethyl-4-methylthioquinazoline, long yellowish needles, m. 138°. Heating 13 g. N-(2-naphthyl)benzimide chloride in 50 cc. PhCN with 6.8 g. AlCl₃ 20 min. at 150-60° and adding ice-H₂O give 87.5% 2,4-diphenyl-5,6-benzoquinazoline, needles, m. 153°; 7,8-benzo isomer, 90.5%, m. 160°. That ring closure occurs at the 1- and not at the 3-position is shown by the fact that N-(α-chloro-2-naphthyl)-benzimide chloride under the same conditions does not give a quinazoline. Adding 4 g. SnCl₄ to 5 g. Ph₂N₂C and 5.5 g. IV in 60 cc. o-C₆H₄Cl₂, heating the mixture 0.5 hr. at 160°, and pouring it onto ice gives 95.5% 2-phenyl-4-diphenylaminoquinazoline hexachlorostannate, fine deep yellow needles, m. 276-9°, which, boiled with alkali, gives the free base, shiny leaflets, m. 156°. Heating 5 g. NCCO₂Et, 11.5 g. IV, and 13 g. SnCl₄ in 30 cc. o-C₆H₄Cl₂ 10 min. at 140°, adding 20% NaOH, steam distilling, and acidifying the hot filtered solution with dilute HCl gives 52% 2-phenylquinazoline-4-carboxylic acid, pale yellow crystals, m. 151° (CO₂ evolution). Heating 7.5 g. N-(vic-m-xylyl)benzonitrilium tetrachloroaluminate and 2.1 g. PhCN in 15 cc. o-C₆H₄Cl₂ 10 min. at 150° gives 62.5% [2,6-Me₂C₆H₃N:CPhN:CPh]AlCl₄, yellow crystals, m. above 400°; the corresponding ZnCl₃ compound, 67.5%, yellow crystals; both compds. decompose with H₂O with the formation of 2,6-Me₂C₆H₃NHBz, m. 172°. Warming 15.5 g. PhN₂BF₄ (VII) with 30 cc. MeCNS slowly to 70° causes a vigorous reaction; keeping the temperature below 100° and then heating it 5 min. at 110° gives 41% 2,4-dimethylthioquinazoline (VIII).BF₄, m. 205° (decomposition) (free base,

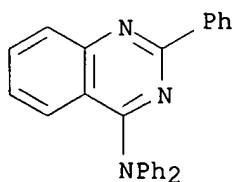
needles, m. 67-8°; picrate m. 171°); with PhN2.SnCl6 in lieu of VII 54.5% VIII is obtained; 6-Me homolog (IX) of VIII, 49%, m. 104-5°. Heating V with alc. NH3 1 hr. at 150° gives o-C6H4.N:CR.N:CR' (X, R = Ph, R' = NH2), 100%, m. 142-3°. V and CuCN boiled 8 hrs. in PhNO2 gives 87% X (R = Ph, R' = CN), m. 166-7°. VIII boiled 2 hrs. with 10% alc. KOH gives 92% X (R = MeS, R' = OH), m. 219°; 3hrs. with 4% alc. NaOMe gives 85% OMe analog, m. 56°; VIII 3 hrs. at 150° with saturated alc. NH3, 81% NH2 analog, m. 233-4°; VIII 2 hrs. with 5% PhNH2-EtOH, 85% X (R = MeS, R' = PhNH), m. 179°. VIII and saturated alc. NH3 at 230° gives 81% X (R = R' = NH2), m. 249-50°. The following addnl. X are prepared (R, R', % yield, m.p. given): Ph, 2-ClC6H4, 90.5, 163°; Ph, CC13, 32.5, 109°; CC13, Ph, 78.8, 129°; CC13, 2-ClC6H4, 62.5, 133°; CC13, CC13, 18.5, 133°; CHCl2, Ph, 74.4, 185°; CH Cl12, 2-ClC6H4, 51.5, 134°. The following quinazolines were prepared: 8-methyl-2,4-diphenyl, 97.5%, m. 124.5°; 6,8-dichloro-2,4-diphenyl, 94%, m. 200-1°; 8-methyl-2-phenyl-4-benzyl, 73.5%, m. 183-4°; 6-chloro-2-phenyl-4-benzyl, 83.3%, m. 195°; 6,8-dichloro-2-phenyl-4-diphenylmethyl, 75.5%, m. 310°. The following X are prepared by heating the appropriate aryl diazonium fluoborate: 2,4-diphenyl, 58%, m. 119-20°; 6-Me homolog, 69.5%, m. 177°; 6-Cl analog, 78%, m. 184-5°; 5,6- or 6,7-Me2 homolog, 22%, m. 173-4°; 5,7-Me2 homolog, 57.5%, m. 154-5°; 2,4-dibenzyl-5,8-dimethyl, 42%, m. 98-9°. Heating 22 g. 2,5-Me2C6H3N2BF4 with 20 cc. MeCN at 60-70° until the N evolution has ceased and keeping the mixture 2 days give 51.5% bisfluoborate of the 2',5'-dimethylanil of 2,5,8-trimethyl-4-acetonylquinazoline (XI), yellow crystals, m. above 200° (free base, liberated with NaOH, yellow plates, m. 126-7°; di-HCl salt, m. 148-50°; monopicrate, brick-red crystals, m. 180°; methiodide, red-yellow prisms, m. 215°). Heating with acids splits XI into p-xylidine and 2,5,8-trimethyl-4-acetonylquinazoline, yellowish needles, m. 135° (picrate, m. 205°). In 2 of 10 expts. the primarily formed 2,4,5,8-tetramethylquinazoline was obtained in small yield and isolated as the picrate, yellow needles, m. 207-8°. Warming sym-m-xylyl-, asym-o-xylyl-, and pseudocumyldiazonium fluoborates with MeCN gives the corresponding anils in 64, 53, and 63% yield, resp. Treating 10.8 g. IV in 30 cc. MeCN with 6.7 g. AlCl3 and heating the mixture a few min. at the boil give 88% anil (XII) of 2-phenyl-4-phenacylquinazoline, yellow crystals, m. 214-15°, also obtained when equimolar amts. of II and IV are condensed in PhNO2 in the presence of AlCl3; XII is quite stable toward alkali and acids. When 11.5 g. IV and 4.4 g. NCCH2CO2Et in 30 cc. PhNO2 are treated with 13 g. SnCl4 and the mixture, after the initial exothermic reaction has ceased, is heated 5 min. at 120°, then made alkaline, and steam distilled, 45.5% anil of 2-phenyl-4-(α -carboxyphenacyl)quinazoline, orange-red rosettes, m. 335°, is obtained; it is stable toward boiling alkali and acids.

IT 103051-13-4P, Quinazoline, 4-diphenylamino-2-phenyl-

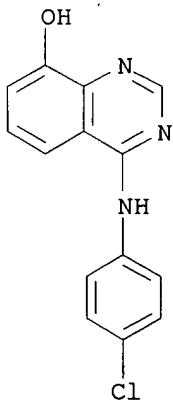
RL: PREP (Preparation)
(preparation of)

RN 103051-13-4 HCAPLUS

CN 4-Quinazolinamine, N,N,2-triphenyl- (9CI) (CA INDEX NAME)

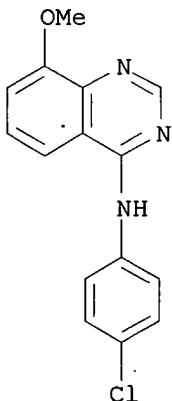


L6 ANSWER 289 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1955:64868 HCPLUS
 DOCUMENT NUMBER: 49:64868
 ORIGINAL REFERENCE NO.: 49:12488h-i
 TITLE: The reactions of 1-chlorophthalazine
 AUTHOR(S): Badger, G. M.; McCarthy, I. J.; Rodda, H. J.
 CORPORATE SOURCE: Univ. Adelaide
 SOURCE: Chemistry & Industry (London, United Kingdom) (1954)
 964
 CODEN: CHINAG; ISSN: 0009-3068
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB The hydrolysis of 1-chlorophthalazine proceeds abnormally with the principal (60%) product being 2-(1-phthalazinyl)-1(2H)-phthalazinone which is achieved if the chlorophthalazine first couples with itself to form an intermediate quaternary salt.
 IT 101094-90-0P, 8-Quinazolinol, 4-p-chloroanilino-
 RL: PREP (Preparation)
 (preparation of)
 RN 101094-90-0 HCPLUS
 CN 8-Quinazolinol, 4-p-chloroanilino- (6CI) (CA INDEX NAME)



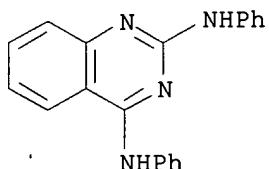
L6 ANSWER 290 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1955:64867 HCPLUS
 DOCUMENT NUMBER: 49:64867
 ORIGINAL REFERENCE NO.: 49:12488g-h
 TITLE: Synthesis, of potential amebicidal agents
 AUTHOR(S): Iyer, R. N.; Anand, Nitya; Dhar, M. L.
 CORPORATE SOURCE: Central Drug Research Inst., Lucknow
 SOURCE: Journal of Scientific & Industrial Research (1954),
 13B, 451-2
 CODEN: JSIRAC; ISSN: 0022-4456
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB The preparation and study of some 4-substituted 8-hydroxyquinazolines (I) as potential amebicidal agents are briefly reviewed. Thus 3,2-MeO(H2N)C6H3CO2H (II), prepared from the corresponding nitro compound (Albert and Hampton, C.A. 48, 8231g) by catalytic reduction (Nye and Mitchell, C.A. 42, 6341e), heated with HCONH2 gave 8-methoxy-4-quinazolinone (III), converted into the corresponding 4-Cl compound (IV) with PCl5 or POCl3. IV condensed with various amines gave the I after

demethylation with AlCl₃ in C₆H₆ or by heating with pyridine-HCl.
 IT 100865-50-7P, Quinazoline, 4-p-chloroanilino-8-methoxy-
 RL: PREP (Preparation)
 (preparation of)
 RN 100865-50-7 HCPLUS
 CN Quinazoline, 4-p-chloroanilino-8-methoxy- (6CI) (CA INDEX NAME)



L6 ANSWER 291 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1955:8298 HCPLUS
 DOCUMENT NUMBER: 49:8298
 ORIGINAL REFERENCE NO.: 49:1731g-i,1732a
 TITLE: A new synthesis of 2,4-dianilinoquinazoline
 AUTHOR(S): Dymek, Wojciech
 CORPORATE SOURCE: Univ. Lublin, Pol.
 SOURCE: Ann. Univ. Mariae Curie Skłodowska, Lublin-Polonia,
 Sect. AA (1951), 6(No. 3), 25-30
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 AB PhN:C(NHPh)NH₂ (10 g.) and 8 g. PhN:C:S heated at 220° for 3 hrs., added hot to EtOH, cooled, filtered, and treated with concentrated HCl gave 2,4-dianilinoquinazoline (I) isolated as the hydrochloride, needles from alc., m. 317°. I.HCl was also obtained by heating 12 g. BzNH₂ and 10 g. PhNH₂ for 1 hr. at 200°, then adding 15 g. PhN:C:S, heating for 3 hrs. at 230°, and working up with EtOH and HCl as above. I.HCl with dilute NaHCO₃ gave the hydrate of the free base, needles or rods from dilute alc., m. 65° which, dried in vacuo at 100° gave I, m. 125°; picrate, yellow needles from alc., m. 273°; 2,4-diacetyl dianilinoquinazoline, rods from dilute alc., m. 152°. Saponification of I.HCl with alc. KOH gave 2,4-dihydroxyquinazoline (II), plates from alc., m. 350°. 4.4 g. PhN: C(NH₂)Ph and 6.1 g. PhN:C:S heated at 220-30° for 3 hrs. and worked up as before gave I.HCl and not the expected 2-phenyl-4-anilinoquinazoline. Equimolar quantities of HN₂CSNH₂, PhNH₂, and PhN:C:S heated at 230° for 3 hrs. also gave I, isolated as the picrate. o-NH₂C₆H₄CO₂H (5 g.) and 2.5 g. CO(NH₂)₂ heated for 2 hrs. at 150° gave II. II (3.2 g.), 8 g. PC15, and 10 ml. POCl₃ heated to slow boiling for 0.5 hr., quenched with ice, dissolved in Et₂O, dried with CaCl₂, and distilled under reduced pressure gave 2,4-dichloroquinazoline (III) m. 115°. III in EtOH heated with excess PhNH₂ for 10 min. to boiling gave I, isolated as the HCl salt. It was concluded that the reaction between the NH₂ group and PhN:C:S to form the quinazoline nucleus takes place only if the guanidine structure is present and is impossible with compds. having the amidine structure.

IT 27142-44-5, Quinazoline, 2,4-dianilino-
(and derivs.)
RN 27142-44-5 HCAPLUS
CN 2,4-Quinazolinediamine, N,N'-diphenyl- (9CI) (CA INDEX NAME)



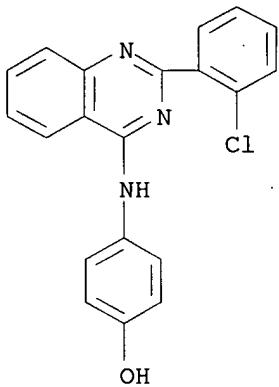
L6 ANSWER 292 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1954:18366 HCAPLUS
 DOCUMENT NUMBER: 48:18366
 ORIGINAL REFERENCE NO.: 48:3369a-g
 TITLE: Antimalarials. I. Quinazoline series
 AUTHOR(S): Dass, Ramji; Vig, O. P.; Gupta, I. S.; Narang, K. S.
 SOURCE: Journal of Scientific & Industrial Research (1952),
 11B, 461-3
 CODEN: JSIRAC; ISSN: 0022-4456
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB o-H₂NC₆H₄CONH₂ (I) was condensed with o- or p-ClC₆H₄COCl (II), and the products cyclized to the quinazolines, and converted with PCl₅ and POCl₃ to the 4-Cl derivs. which were condensed with substituted aryl amines. I (4.4 g.) in 50 ml. C₆H₆ and 10 ml. C₅H₅N slowly treated with 5.0 g. II, the mixture warmed 20 min. on a H₂O bath, filtered, and the residue washed with Na₂CO₃ solution and crystallized from 70% EtOH gave 5 g. o-(o-chlorobenzamido)benzamide (III), m. 199.5°. III (2 g.) in 20 ml. absolute EtOH treated with 0.5 g. KOH, the mixture heated 40 min., diluted with 200 ml. H₂O, cooled, filtered, and the filtrate acidified with HOAc, boiled, cooled, and filtered, gave 1.5 g. 2-(o-chlorophenyl)-4-quinazolinone (IV), m. 183° (from 40% EtOH). PCl₅ (6 g.), 10 ml. POCl₃, and 2 g. IV refluxed 3 hrs., the P compds. removed by vacuum distillation, 15 ml. dry C₆H₆ added, then distilled off, the process repeated, and the product crystallized from 60-80° petr. ether gave 1.0 g. 2-(o-chlorophenyl)-4-chloroquinazoline (V), m. 126°. V (1.0 g.) in 20 ml. dry C₆H₆ added to 1.05 g. PhCH₂NH₂, the mixture refluxed 1 hr., the C₆H₆ removed, the residue crystallized from EtOH containing HCl, the HCl salt washed with Et₂O and C₆H₆, dissolved in EtOH, treated with 2 ml. 1% KOH, and the product crystallized from 9% EtOH gave 1.2 g. 2-(o-chlorophenyl)-4-benzylaminoquinazoline, m. 188°. Similarly were prepared the following 2-(o-chlorophenyl)quinazolines (4-substituent, m.p., and crystallization solvent given): p-toluidino, 170°, absolute EtOH; p-anisidino (HCl salt), 148°, diluted EtOH; p-ethoxyanilino, 234-6°, absolute EtOH; o-toluidino (HCl salt), 174°, 60% EtOH; o-anisidino (HCl salt), 156°, 60% EtOH; o-ethoxy, 146°, 80% EtOH; p-chloroanilino (HCl salt), 257°, 80% EtOH; p-bromoanilino, 197°, absolute EtOH; p-hydroxyanilino (HCl salt), 304°, absolute EtOH; N-methyl-p-toluidino (HCl salt), 258°, absolute EtOH; N-ethyl-p-toluidino (HCl salt), 168.5°, 50% EtOH; N-methyl-o-toluidino (HCl salt), 163°, 40% EtOH; N-ethyl-o-toluidino (HCl salt), 174°, 50% EtOH; N-ethyl-p-methoxyanilino (HCl salt), 182-4°, diluted EtOH. 2-(p-Chlorophenyl)quinazolines (4-substituent, m.p., and crystallization solvent given): benzylamino (HCl salt), 300°, diluted EtOH;

p-anisidino, 158°, 80% EtOH; p-ethoxyanilino, 105°, diluted EtOH; o-toluidino, 145°, absolute EtOH; o-anisidino (HCl salt), 270°, absolute EtOH; o-ethoxyanilino, 177°, diluted EtOH; p-chloroanilino, 197°, 70% MeOH; p-bromoanilino, 220°, C6H6; p-hydroxyanilino (HCl salt), 296°, absolute EtOH; N-methyl-p-toluidino, 170°, diluted EtOH; N-ethyl-p-toluidino-, 181°, absolute EtOH; N-methyl-o-toluidino-, 168°. Me2CO; N-ethyl-o-toluidino, 120°, diluted EtOH; N-ethyl-p-anisidino, 124°, 60% EtOH; and p-toluidino, 148°, 90% EtOH.

IT 347366-40-9, Quinazoline, 2-[o-chlorophenyl]-4-p-hydroxyanilino-
RL: PREP (Preparation)
(hydrochlorides)

RN 347366-40-9 HCPLUS

CN Phenol, 4-[[2-(2-chlorophenyl)-4-quinazolinyl]amino]- (9CI) (CA INDEX
NAME)



L6 ANSWER 293 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:3618 HCPLUS
DOCUMENT NUMBER: 48:3618
ORIGINAL REFERENCE NO.: 48:688c-i,689a
TITLE: Aminolysis of heterocyclic amides. I. The aminolysis
of 6,7-diphenyllumazine
AUTHOR(S): Taylor, E. C., Jr.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1952), 74,
1651-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. following abstract An alkylamine with 6,7-diphenyllumazine (I) gives first an N-substituted amide of a 3-(3-alkylureido)-5,6-diphenylpyrazinoic acid, which can then be converted to an N-substituted amide of 3-amino-5,6-diphenylpyrazinoic acid by further reaction with the amine. The mechanism of these transformations is discussed and the results are interpreted as a substantiation for the ring cleavages previously postulated (cf. C.A. 47, 137h) in the reaction of 4-NH₂ and 4-hydroxy-2-mercaptopteridines with alkylamines. I (3.0 g.) in 20 cc. PhCH₂NH₂ (II) refluxed 15 min. and diluted with 50 cc. absolute EtOH yielded 2.18 g. N-benzyl-3-(3-benzylureido)-5,6-diphenylpyrazinamide (III). EtOH, m. 88-93°; III m. 150-1°. III (0.60 g.), 10 cc. Ac₂O, and 3 g. NaOAc refluxed 2 h., and the cooled mixture poured on ice and let stand overnight yielded III, m. 150-1°. III (0.50 g.) in 10 cc. II

refluxed 8 h., diluted with 20 cc. EtOH, heated to boiling and diluted with water to incipient precipitation yielded 0.348 g. 3-amino-N-benzyl-5,6-diphenylpyrazinamide (IV), m. 188.5-9°; the filtrates from IV concentrated to 20 cc. and diluted with 20 cc. water yielded N,N'-dibenzylurea (V), 168°. I and II refluxed 8 h. yielded directly IV and V.

H₂SO₄ (2 cc.) added slowly to 1.0 g. 3-amino-5,6-diphenylpyrazinoic acid in 15 cc. absolute EtOH, the solution let stand 24 h. at room temperature, and poured

into 75 cc. water yielded 0.91 g. Me ester (VI), m. 204-6°. VI (165 mg.) and 2 cc. II refluxed 10 min., diluted with 15 cc. 50% EtOH and cooled yielded 190 mg. IV, m. 188.5-89°. IV (1.0 g.), 20 cc. 85% HCO₂H, 20 cc. Ac₂O, and 1.0 g. NaOAc refluxed 5 h. and the solution evaporated to dryness yielded 0.42 3-benzyl-6,7-pteridin-4(3H)-one, m. 248°. I (0.50 g.) and 15 cc. morpholine refluxed 14 h. yielded 0.53 g.

3-(morpholinocarbonylamino)-5,6-diphenylpyrazinoic acid morpholide (VII), m. 262-4°. VII (1.0 g.) sealed in 20 cc. morpholine heated 12 h. at 140° and 6 h. at 190° yielded 0.64 g.

3-amino-5,6-diphenylpyrazinoic acid morpholide (VIII), m. 190.5-1°. I and morpholine heated 12 h. at 190° yielded VIII directly. I (3.0 g.), 30 cc. piperidine, and 10 cc. HCONMe₂ refluxed 16 h., filtered, and the hot filtrate treated with boiling water to incipient turbidity yielded 1.67 g. 3-(piperidinocarbonylamino)-5,6-diphenylpyrazinoic acid piperidide, m. 215-17°. I (5.0 g.) in 50 cc. piperidine heated 20 h. at 200° yielded 3.8 g. 3-amino-5,6-diphenylpyrazinoic acid piperidide, m. 156°. I (0.50 g.) in 15 cc. HOCH₂CH₂NH₂ refluxed 12 h. yielded 0.453 g. 3-amino-N-(β-hydroxyethyl)-5,6-diphenylpyrazinamide, m. 186.5-87°. I (2.0 g.) and 40 cc. NH₄OH heated 16 h. at 185° yielded 1.67 g. 3-amino-5,6-diphenylpyrazinamide (IX), m. 203.5-5°. IX (0.3 g.) and 1 cc. II refluxed 15 min., diluted with 10 cc. EtOH, and hot water added to incipient crystallization yielded 0.31 g. IV. IX (0.06 g.), 5 cc. piperidine, and 2 cc. HCONMe₂ refluxed 16 h. yielded 0.053 g. IX, m. 203.5-5°.

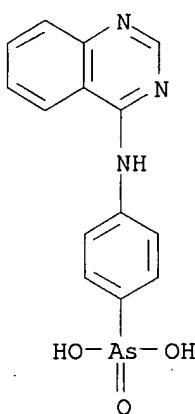
p-O₂NC₆H₄NHCONH₂ (2.0 g.) and 20 cc. piperidine refluxed 8 h. yielded 2.43 g. 1-(p-nitrophenyl)-3-(piperidino)urea, m. 165-6°. I (1.0 g.) and 10 cc. 85% H₄N₂.H₂O refluxed 6 h. and the mixture let stand 3 h. at 0° yielded 0.705 g. 3-amino-5,6-diphenylpyrazinoic acid hydrazide (X), m. 250-1°. The mother liquors from X evaporated to dryness, the residue washed with water, dried, extracted with CH₂Cl₂, and the extract diluted with petr. ether yielded 3-amino-6,7-diphenyl-2,4(1H,3H)-pteridinedione, m. 259-60° (decomposition); evaporation of the filtrates yielded about 0.015 g. X.

IT 860720-53-2P, Arsanilic acid, N-4-quinazolinyl-

RL: PREP (Preparation)
(preparation of)

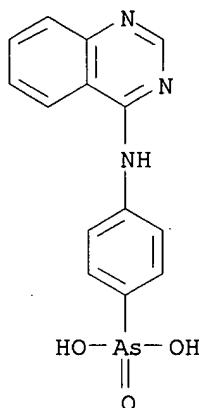
RN 860720-53-2 HCAPLUS

CN Quinazoline, 4-p-arsonoanilino- (5CI) (CA INDEX NAME)



L6 ANSWER 294 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1954:3617 HCPLUS
 DOCUMENT NUMBER: 48:3617
 ORIGINAL REFERENCE NO.: 48:687h-i,688a-c
 TITLE: Arsenicals containing quinoline and quinazoline nuclei
 AUTHOR(S): Wu, Yao-Hua; Hamilton, Cliff S.
 CORPORATE SOURCE: Univ. of Nebraska, Lincoln
 SOURCE: Journal of the American Chemical Society (1952), 74,
 1863-4
 CODEN: JACSAT; ISSN: 0002-7863
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB 4-Hydroxy-x-nitroquinazoline (3.8 g.) added portionwise to 20.3 g.
 $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ in 30 cc. warm HCl, the mixture refluxed 1 h., diluted with water, neutralized with CaCO_3 , heated to boiling and filtered hot yielded the following x-amino-4-hydroxyquinazoline, x, % yield, and m.p. given: 5, 76.4, 236°; 6, 67.0, 316°; 7, 53.7, 315°. The amine (3.5 g.) in 35 cc. 2N HCl below 5° treated with NaNO_2 , the diazonium solution poured into water containing 3 g. NaOH, 5 g. Na_2HAsO_3 , and a few crystals of CuSO_4 , the mixture stirred 2 h., let stand overnight, warmed 10 min. at 80°, filtered, the filtrate neutralized with HCl, treated with C, made acid to Congo red with HCl and filtered yielded the arsonic acid. The arsonic acid (1 g.) in 35 cc. 1.5N HCl containing a trace of KI saturated with SO_2 (ice bath) 2 h., the mixture refrigerated 2 h., neutralized with NH_4OH , the precipitate dissolved in N NaOH and the solution treated with CO_2 yielded the arsenoso derivative. The 4-chloroquinoline or 4-chloroquinazoline (0.005 mol) and 0.0045 mol p-H₂NC₆H₄AsO(OH)₂ in 5 cc. Me₂NOCH at 50° were heated 3-4 h. at 80-90°. The compds. prepared, m.p., and % yield are: 4-hydroxyquinoline-6-arsonic acid, 320°, 29.7; 4-hydroxy-2-methylquinoline-6-arsonic acid, above 320°, 31.6; 4-hydroxyquinazoline-5-arsonic acid, above 320°, 48.3; 4-hydroxyquinazoline-6-arsonic acid, above 320°, 22.2; 4-hydroxyquinazoline-7-arsonic acid, above 320°, 42.2; 6-arsenoso-4-hydroxyquinoline, 317°, 53.2; 6-arsenoso-4-hydroxy-2-methylquinoline, 310°, 75.1; 7-arsenoso-4-hydroxyquinazoline, 295°, 69.1; 4-(4-arsonoanilino)-8-nitroquinoline, 288°, 30.2; 4-(4-arsonoanilino)-2-methylquinoline, 285°, 33.2; 4-(4-arsonoanilino)-2-methyl-6-nitroquinoline, 288°, 50.1; 4-(4-arsonoanilino)quinazoline, above 320°, 58.
 IT 860720-53-2P, Arsanilic acid, N-4-quinazolinyl-
 RL: PREP (Preparation)
 (preparation of)

RN 860720-53-2 HCAPLUS
 CN Quinazoline, 4-p-arsenoanilino- (5CI) (CA INDEX NAME)



L6 ANSWER 295 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1953:12395 HCAPLUS

DOCUMENT NUMBER: 47:12395

ORIGINAL REFERENCE NO.: 47:2217e-f

TITLE: 10-(2-Dialkylaminoethyl)phenothiazine

INVENTOR(S): Nishijo, Shigeya; Nishimura, Aki

PATENT ASSIGNEE(S): Nippon Chemical Industries Co.

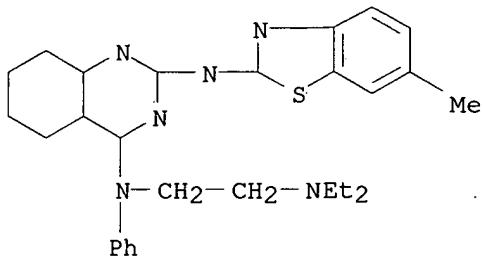
DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

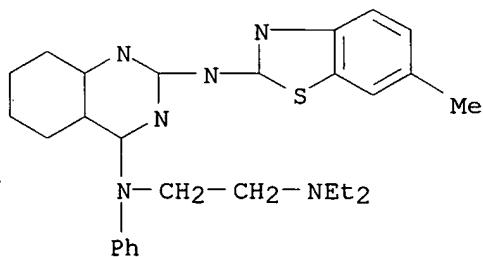
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|---|----------|-----------------|------|
| | JP 25001134 | B4 | 19500331 | JP | |
| AB | Phenothiazine (65 g.) in 700 mL. C6H6 refluxed 4 h. with 50 g. NaNH2, 70 g. Me2N(CH2)2Cl added, the mixture refluxed 12 h., cooled, filtered, the filtrate shaken with HCl, the aqueous layer made alkaline with NaOH, extracted with ether, and the extract distilled yielded 78 g. 10-(2-dimethylaminoethyl)phenothiazine, b1.5 190-7° (HCl salt, columns, m. 225°); 10-(2-diethylaminoethyl) analog, b1.5 195-7° (HCl salt, m. 186°). | | | | |
| IT | 873407-61-5P | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- | | | |
| | RL: PREP (Preparation)
(preparation of) | | | | |
| RN | 873407-61-5 | HCAPLUS | | | |
| CN | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) | (CA INDEX NAME) | | | |



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L6 ANSWER 296 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1953:12394 HCAPLUS
 DOCUMENT NUMBER: 47:12394
 ORIGINAL REFERENCE NO.: 47:2217e
 TITLE: 2,4-Disubstituted amino quinazolines
 INVENTOR(S): Isler, Hans; Hueni, Albrecht
 PATENT ASSIGNEE(S): Ciba Pharmaceutical Products, Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|---|----------|-----------------|----------|
| | ----- | ----- | ----- | ----- | ----- |
| AB | US 2623878 | | 19521230 | US 1949-73435 | 19490128 |
| AB | See Brit. 664,262 (C.A. 47, 617b). | | | | |
| IT | 873407-61-5P | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- | | | |
| | | RL: PREP (Preparation) | | | |
| | | (preparation of) | | | |
| RN | 873407-61-5 | HCAPLUS | | | |
| CN | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- | (5CI) (CA INDEX NAME) | | | |



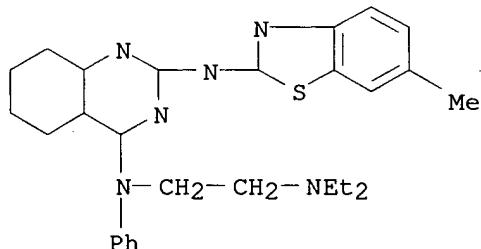
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L6 ANSWER 297 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1953:12393 HCAPLUS
 DOCUMENT NUMBER: 47:12393
 ORIGINAL REFERENCE NO.: 47:2217c-e
 TITLE: Vitamin B6 derivatives
 INVENTOR(S): Heyl, Dorothea
 PATENT ASSIGNEE(S): Merck & Co., Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| | US 2583774 | | 19520129 | US 1948-24412 | 19480430 |
| AB | The acetoxime of 3-acetoxy-5-acetoxymethyl-4-formyl-2-methylpyridine (I), m. 114.5-15°, refluxed 2 h. with Ac ₂ O, gives the 4-cyano analog (II) of I, m. 63-4°. II, refluxed 2 h. in EtOH containing 0.1% Na, gives the 3-HO analog (III) of II, m. 209-10°. III with 3 N KOH gives 4-carboxy-3-hydroxy-5-hydroxymethyl-2-methylpyridine (IV), m. 253-4° (decomposition). IV, refluxed with EtOH containing anhydrous HCl, gives the lactone of IV, m. 273-3.5° (decomposition). Alternatively, 5-chloromethyl-4-cyano-3-hydroxy-2-methylpyridine, m. 167-8° (decomposition), is hydrolyzed to 4-carbamyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine-HCl, m. 210-11° (decomposition), which in turn gives IV. The lactone has growth-promoting and antianemia activity. Cf. C.A. 44, 10740c. | | | | |
| IT | 873407-61-5P, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- | | | | |
| | RL: PREP (Preparation)
(preparation of) | | | | |
| RN | 873407-61-5 HCPLUS | | | | |
| CN | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME) | | | | |



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L6 ANSWER 298 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1953:10813 HCPLUS
 DOCUMENT NUMBER: 47:10813
 ORIGINAL REFERENCE NO.: 47:1940g-i,1941a-e
 TITLE: Dyeing of wool with metalized azo dyes in the presence of an aldehyde having an affinity for wool
 INVENTOR(S): Widmer, Willy; Buehler, Arthur; Roesti, Hans
 PATENT ASSIGNEE(S): C I B A Ltd.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|------|
| | US 2602722 | | 19520708 | US | |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | Chromated dyes from o-hydroxy-o'-amino monoazo dyes sensitive to demetallization by acids are dyed on wool preferably in the presence of a colorless H ₂ O-soluble aldehyde (I) having an affinity for wool of at least 60% and a H ₂ O-soluble monoazo dye (II) having an aldehyde group and giving a | | | | |

yellow dyeing. Thus, to a neutral solution of p-H₂NC₆H₄SO₃Na 19.5 parts in H₂O 200 is added dropwise at 0-5° within 0.5 hr. cyanuric chloride 18 suspended in H₂O 800, to the mixture is added in the course of 3 hrs. Na₂CO₃ 5.3 in H₂O and then m-H₂NC₆H₄CHO (III) 12.1 in hot (60°) H₂O 600 and 30% HCl 11.5 in the course of 0.5 hrs., the mixture neutralized with stirring at 30-40° with Na₂CO₃ 10.6 in H₂O over a period of 10 hrs., 27% aqueous NH₃ 6.5 added, the mixture heated within 1 hr. to 96-8°, then refluxed 2 hrs. and filtered, the hot filtrate made weakly acidic with HCl and cooled, the resulting slimy mass separated, stirred in H₂O 200 parts, dissolved by neutralizing with aqueous NaHCO₃, and the solution

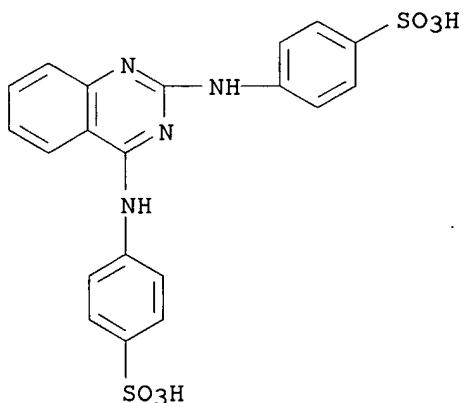
evaporated to give IV, X = H (V), slightly brownish solid. The following I are prepared similarly: from 4,4'-diamino-2,2'-biphenyl disulfonic acid is obtained VI; from 3,6-H₂N(HO₃S)C₆H₃CHO and III is obtained IV, X = CHO (VII). Into 4,2-H₂N(NaO₃S)C₆H₃CHO 24.5 parts in H₂O 350 is introduced in the course of 6-8 hrs. at 20-5° COCl₂ 2, the liberated HCl is neutralized by adding dilute aqueous Na₂CO₃, and there is obtained (4,3-OHC(NaO₃S)C₆H₃NH)₂CO (VIII), slightly brownish colored substance. Another I is obtained from 2,4-dichloroquinazoline III, and p-H₂NC₆H₄SO₃Na. The Cr complex of the dye (IX) from diazotized 2,5-H₂N(O₂N)C₆H₃OH and 2,6-H₂NC₁₀H₆SO₃H is dyed on wool in the presence of V, VI, VII, and VIII to give a level pure green tint (IX from an acid bath dyes a duller and bluer shade). If the dyeings with IX are carried out in the presence of a I and a II, somewhat yellower green tints are obtained. Examples for the use of II of the type m-OHCC₆H₄N:NC:C(OH).NAr.N:CX, where X is Me or CO₂H, and Ar is m-HO₃SC₆H₄, 2,5,4-Cl₂(SO₃Na)C₆H₂, 4,1-HO₃SC₁₀H₆, 2,5-Cl(HO₃S)C₆H₃, 2,4-Me(HO₃S)C₆H₃, are given. The II are obtained by coupling diazotized III with the corresponding 1-aryl-3-methyl-5-pyrazolones.

IT 858235-78-6P, Quinazoline, 2,4-bis(p-sulfoanilino)-

RL: PREP (Preparation)
(preparation of)

RN 858235-78-6 HCPLUS

CN INDEX NAME NOT YET ASSIGNED



L6 ANSWER 299 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1953:3470 HCPLUS

DOCUMENT NUMBER: 47:3470

ORIGINAL REFERENCE NO.: 47:617b-h

TITLE: Heterocyclically substituted diaminoquinazolines

PATENT ASSIGNEE(S): C I B A Ltd.

DOCUMENT TYPE: Patent

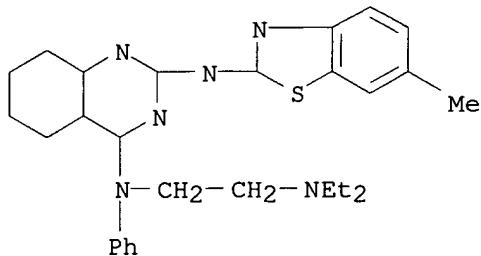
LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| | GB 664262 | | 19520102 | GB 1949-3339 | 19490207 |
| AB | 2,4-Diaminoquinazolines substituted by a thiazolyl or imidazolyl group on one of the NH ₂ groups and by a dialkylaminoalkyl group on the other, prepared by standard methods, are useful as medicinals, some being antituberculars. 2-(Substituted amino)-4-(2-diethylaminoethylamino)quinazolines (substituent on the 2-NH ₂ given): 2-thiazolyl, m. 142-3° (HCl salt, m. 297-8°); 4-phenyl-2-thiazolyl, m. 172-4°; 4-p-tolyl-2-thiazolyl, m. 181-3°; 4,5-diphenyl-2-thiazolyl, m. 198-202° (dimethanesulfonate, m. 290-2°); 2-benzothiazolyl, m. 216-18° (HCl salt, m. 305-7°); 4-methyl-2-benzothiazolyl, m. 193-5°; 6-methyl-2-benzothiazolyl, m. 189-91° (HCl salt, m. 296-8°); 4,7-dimethyl-2-benzothiazolyl, m. 205-7° (HCl salt, m. 339-42°); 6-methoxy-2-benzothiazolyl, m. 186-7° (HCl salt, m. 293-5°); 6-butoxy-2-benzothiazolyl, m. 168-9° (HCl salt, m. 273-5°); 6-cyano-2-benzothiazolyl, m. 289-92° (HCl salt, m. 305-7°; dimethanesulfonate, m. 299-300°); 6-acetamido-2-benzothiazolyl, m. 252-7° (HCl salt, m. 317-19°); 6-nitro-2-benzothiazolyl, m. 304-6°; 6-chloro-2-benzothiazolyl, m. 210-11° (HCl salt, m. 310-11°; dimethanesulfonate, m. 302-4°); 6,7-benzo-2-benzothiazolyl, m. 220-2°; 2-benzimidazolyl, m. 224-5°; 6-methyl-2-benzimidazolyl, m. 225-7°. 2-(Substituted amino)-6-chloro-4-(2-diethylaminoethylamino)quinazolines: 2-thiazolyl, m. 180.5-1° (HCl salt, m. 286-8°); 6-methyl-2-benzothiazolyl, m. 226-8°; 6-methoxy-2-benzothiazolyl, m. 197-8° (HCl salt, m. 299-300°); 2-benzimidazolyl, m. 196-7°. Other quinazolines: 2-(6-methyl-2-benzothiazolylamino)-4-(3-diethylaminopropylamino), m. 202-4°; 2-[4-(p-bromophenyl)-2-thiazolylamino]-4-(3-diethylamino-1-methylpropylamino), m. 219-21° (HCl salt, m. 312-14°); 2-(6-methyl-2-benzothiazolylamino)-4-(3-diethylamino-1-methylpropylamino), m. 142-3° (HCl salt, m. 295-6°); 2-(2-diethylaminoethylamino)-4-(6-methyl-2-benzothiazolylamino), m. 239-41°; 2-(6-methyl-2-benzothiazolylamino)-4-[2-(1-piperidyl)ethylamino], m. 204-6° (HCl salt, m. 343-4°; dimethanesulfonate, m. 312-13°); 2-(6-acetamido-2-benzothiazolylamino)-4-[p-(2-diethylaminoethoxy)anilino], m. 166-70° (HCl salt, m. 292-7°); 2-(2-benzothiazolylamino)-4-[phenyl(2-diethylaminoethyl)amino], m. 168-9° (HCl salt, m. 278-80°); 2-(6-methyl-2-benzothiazolylamino)-4-[phenyl(2-diethylaminoethyl)amino], m. 180-2°; 2-(6-methyl-2-benzothiazolylamino)-4-[2-(2-diethylaminoethylthio)ethylamino], m. 191-3°. Intermediate 2-chloroquinazoline HCl salts: 4-[phenyl(2-diethylaminoethyl)amino], m. 239-41°; 4-[p-(2-diethylaminoethoxy)anilino], m. 211-13°; 4-(3-diethylamino-1-methylpropylamino), m. 165-7°; 4-[2-(2-diethylaminoethylthio)ethylamino], m. 102-4° (free base). Intermediate 4-hydroxyquinazolines: 2-(2-diethylaminoethylamino)-HCl, m. 201-3°; 2-(6-methyl-2-benzothiazolylamino), m. above 320°. 2-Amino-4,7-dimethylbenzothiazole, m. 158-60°. Most of the HCl salts melt with decomposition | | | | |
| IT | 873407-61-5P, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- | | | | |
| | RL: PREP (Preparation) | | | | |
| | (preparation of) | | | | |
| RN | 873407-61-5 HCAPLUS | | | | |
| CN | Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2- | | | | |

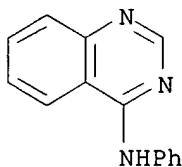
benzothiazolylamino)- (5CI) (CA INDEX NAME)



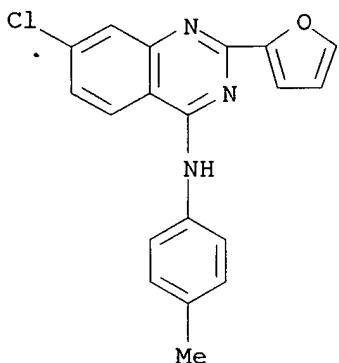
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L6 ANSWER 300 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1952:65348 HCPLUS
 DOCUMENT NUMBER: 46:65348
 ORIGINAL REFERENCE NO.: 46:10883f-i,10884a-b
 TITLE: Ultraviolet absorption spectra of some derivatives of quinoline, quinazoline, and cinnoline
 Hearn, J. M.; Morton, R. A.; Simpson, J. C. E.
 AUTHOR(S):
 CORPORATE SOURCE: Univ. Manchester, UK
 SOURCE: Journal of the Chemical Society (1951) 3318-29
 CODEN: JCSOA9; ISSN: 0368-1769
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB The absorption spectra of 4-hydroxy-, 4-hydroxy-6-nitro-, and 4-aminoquinolines have been compared with those of related compds. of fixed structure, 1-methyl-4-quinolone, 4-methoxyquinoline, 1-methyl-6-nitro-4-quinolone, 4-methoxy-6-nitroquinoline, 6-nitro-4-phenoxyquinoline, 4-hydroxy-3-quinoliniccarboxylic acid, 4-hydroxy-6-methoxy-3-quinoliniccarboxylic acid, 5-amino-, 6-amino-, 4-acetamido-, and 4-anilinoquinoline, 4-amino-6-nitro-, 4-acetamido-6-nitro-, 4-anilino-6-nitro-, and 4-chloro-6-nitroquinoline. Similar investigations have been made on the quinazoline and cinnoline derivs., 4-hydroxy-, 4-methoxy-, and 4-phenoxyquinazoline, 1-methyl- and 3-methyl-4-quinazolone, 4-hydroxy-6-nitroquinazoline, 1-methyl- and 3-methyl-6-nitro-4-quinazolone, 4-methoxy- and 4-phenoxy-6-nitroquinazoline, 4-amino-, 4-acetamido-, and 4-anilinoquinazoline, 4-amino-, 4-acetamido-, and 4-anilino-6-nitroquinazoline, 4-hydroxy- and 4-methoxycinnoline, 1-methyl-4-cinnolone, 4-phenoxy- and 4-ethoxycinnoline, 4-hydroxy-6-nitrocinnoline, 1-methyl-6-nitro-4-cinnolone, 4-methoxy- and 4-phenoxy-6-nitrocinnoline, 3-methyl- and 3-ethyl-4-hydroxycinnoline, 6,7-dimethyl-4-hydroxycinnoline, 3-methyl-6-nitro-4-hydroxycinnoline, 4-hydroxy-3-cinnoline-carboxylic acid, 4-hydroxy-6-methoxy-3-cinnoliniccarboxylic acid, 4-hydroxy-6,7-methylenedioxycinnoline, 6-methyl- and 6-bromo-3-chloro-4-hydroxycinnoline, 3,6-dibromo-4-hydroxycinnoline, methyl 4,6,7-trimethoxy-3-cinnolylacetate, methyl 6,7-dimethoxy-1-methyl-3-cinnolone-4-yacetate, tetrahydro-4,6-diketocinnoline 6-oxime methyl ether N-oxide, 6-methyl- and 6,7-dimethyl-4-acetoxy-3-chlorocinnoline, 6-chloro- and 6-nitro-4-acetoxy-4-cinnoline, 4-amino-, 4-acetamido-, and 4-anilino-4-cinnoline, 4-amino-, 4-acetamido-, and 4-anilino-6-nitrocinnoline. The absorption curves show that when alternative formulations are possible, quinolone, quinazolone and cinnolone structures tend to be predominant.
 IT 34923-95-0, Quinazoline, 4-anilino-
 (spectrum of)
 RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 301 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1951:21795 HCAPLUS
 DOCUMENT NUMBER: 45:21795
 ORIGINAL REFERENCE NO.: 45:3852g-i,3853a
 TITLE: Furylquinazolines. IV. Nucleophilic reactivity of the 2-furyl-4-alkoxyquinazolines
 AUTHOR(S): Andrisano, R.; Modena, G.
 CORPORATE SOURCE: Univ. Bologna, Italy
 SOURCE: Bollettino Scientifico della Facolta di Chimica Industriale di Bologna (1950), 8, 7-9
 CODEN: BSFCAY; ISSN: 0366-3205
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. preceding abstract 2-Furyl-4-chloroquinazoline (I) (C.A. 45, 1600f), refluxed for 0.5 hr. with 0.05 atom Na in 20-30 cc. of an aliphatic alc., poured into H₂O after cooling, and extracted with Et₂O, yields the corresponding 4-alkoxy derivative Thus, the following 2-furyl-4-alkoxyquinazolines (II) are prepared: MeO, prisms from ligroin, m. 65° (picrate, prisms from EtOH, m. 170°); EtO, needlelike prisms from ligroin, m. 83° (picrate, prisms from EtOH, m. 183.4°); PrO, characterized as the picrate, needlelike prisms from EtOH, m. 143.5°; iso-PrO, characterized as the picrate, prisms from EtOH, m. 164°. Similarly, by refluxing 0.02 mol. I, 0.05 atom Na, 8 cc. PhCH₂OH, and 20 cc. dioxane for 1 hr. was prepared 2-furyl-4-benzyloxyquinazoline (III), oil, characterized as the picrate, prisms from EtOH, m. 171°. Also, 2-furyl-4-phenoxyquinazoline (IV), prisms from ligroin, m. 135°. These compds. are hydrolyzed to 2-furyl-4-hydroxyquinazoline by refluxing with aqueous NaOH until they are completely dissolved; the rate of hydrolysis decreases in the order II > IV > III. Refluxing II, III, or IV with a Na alcoholate in the corresponding alc. or in dioxane yields the corresponding 4-alkoxy derivative In general, II are converted to their higher or lower homologs; IV easily yields II and III, but is not formed by this reaction. IV (3.3 g.) and 3 g. Et₂N(CH₂)₃CHMeNH₂ heated at 150° for 1.5 hrs., washed with 10% aqueous NaOH, and distilled in vacuo, yield 2-furyl-4-(5-diethylamino-2-pentylamino)quinazoline, characterized as the picrate, needles from EtOH, m. 179°.
 IT 858236-39-2P, Quinazoline, 7-chloro-2-(2-furyl)-4-p-toluidino-
 RL: PREP (Preparation)
 (preparation of)
 RN 858236-39-2 HCAPLUS
 CN Quinazoline, 7-chloro-2-(2-furyl)-4-p-toluidino- (5CI) (CA INDEX NAME)



L6 ANSWER 302 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1951:21794 HCAPLUS

DOCUMENT NUMBER: 45:21794

ORIGINAL REFERENCE NO.: 45:3852c-g

TITLE: Furylquinazolines. III. 4-Substituted
2-furyl-4-chloroquinazolines

AUTHOR(S): Andrisano, R.; Modena, G.

CORPORATE SOURCE: Univ., Bologna, Italy

SOURCE: Gazzetta Chimica Italiana (1950), 80, 321-4

CODEN: GCITA9; ISSN: 0016-5603

DOCUMENT TYPE: Journal

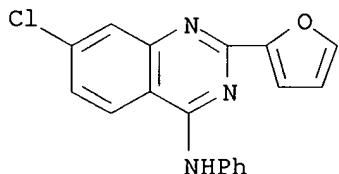
LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 45:21794

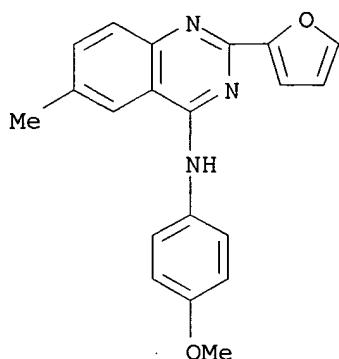
AB cf. C.A. 45, 1601d; following abstract In view of the high anti-malarial power of 4-(4-diethylamino-1-methylbutylamino)-7-chloroquinazoline (cf. Price, et al., C.A. 40, 5747.4), its 2-(2-furyl) derivative (I) was prepared 4,2-Cl(H2N)C6H3CO2H (10 g.) and 12 g. Et 2-furancarboximidate [cf. Ber. 25, 1416(1892)], heated 2 hrs. at 200°, the product taken up in MeOH, filtered, and the residue purified by AcOH, yield 2-(2-furyl)-4-hydroxy-7-chloroquinazoline (II), m. 276°. II (10 g.) in 80 cc. POCl3 and 14 g. PCl5, refluxed 90 min., distilled in vacuo, the residue taken up in ice water, neutralized with NH4OH, filtered, and the residue extracted with C6H6, yields 9.5 g. (88%) of 2-(2-furyl)-4,7-dichloroquinazoline (III), m. 137°. III (5.3 g.) and 6.4 g. H2NCHMeCH2CH2CH2NET2 in 80 cc. C6H6, neutralized by Na2CO3, refluxed 3 hrs., and the product steam-distilled, yield almost 100 % I, m. 112°. With alc. picric acid, it forms a picrate, C33H33O15N10Cl, m. 199°. Since the Cl in the 4-position in III, like that in the chloroquinazolines already described (cf. C.A. 45, 1600f) is reactive with nucleophilic agents, 6 compds. were prepared by replacement of the Cl. III (0.01 mol.) and NaOMe (from 0.03 atom Na in 40 cc. MeOH), refluxed 30 min., diluted with water, and the precipitate purified by ligroin, yields 2-(2-furyl)-4-methoxy-7-chloroquinazoline, m. 130°. III (0.01 mol.) in 20 cc. dioxane and NaOPh (from 0.03 atom Na in 12 g. PhOH), refluxed 30 min., poured into water, NaOH added, and the precipitate purified by aqueous EtOH, yield 100% of the 4-phenoxy analog, m. 140°. Four arylamino derivs. were prepared in high yields by refluxing 0.01 mol. III and 0.02 mol. of the resp. arylamine 1 hr. in C6H6, making alkaline with Na2CO3, and steam-distilling 2-(2-Furyl)-4-phenylamino-7-chloroquinazoline, m. 170° (from EtOH); 4-tolylamino analog, m. 201° (from ligroin); 4-methoxyphenylamino analog, m. 189° (from EtOH); 4-ethoxyphenylamino analog, m. 180° (from EtOH).

IT 860191-83-9P, Quinazoline, 4-anilino-7-chloro-2-(2-furyl)-

RL: PREP (Preparation)
 (preparation of)
 RN 860191-83-9 HCPLUS
 CN Quinazoline, 4-anilino-7-chloro-2-(2-furyl)- (5CI) (CA INDEX NAME)



L6 ANSWER 303 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1951:8789 HCPLUS
 DOCUMENT NUMBER: 45:8789
 ORIGINAL REFERENCE NO.: 45:1601c-g
 TITLE: Furylquinazolines. II. 4-Substituted
 2-furyl-6-methylquinazolines
 AUTHOR(S): Andrisano, R.; Modena, G.
 CORPORATE SOURCE: Univ., Bologna, Italy
 SOURCE: Bollettino Scientifico della Facolta di Chimica
 Industriale di Bologna (1950), 8, 1-3
 CODEN: BSFCAY; ISSN: 0366-3205
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. preceding abstract 5,2-Me(H2N) C6H3CO2Me (22 g.) and 24 g. Et
 2-furanacetimidate (cf. Pinner, Ber. 25, 1416(1892)), heated at
 200° for 1.5 hrs., taken up in MeOH after cooling, filtered,
 washed, and dried, yield 18.5 g. (61%) 2-furyl-4-hydroxy-6-
 methylquinazoline (I), silky needles from EtOH, m. 257°. I (16.8
 g.) is refluxed with 100 cc. POCl3 and 24 g. PC15 for 1.5 hrs., the excess
 POCl3PC15 removed under reduced pressure, the residue taken up with H2O
 and ice, neutralized with NH4OH, filtered, washed, and dried to yield
 after recrystn. from C6H6 14 g. (77%) 4-Cl analog (II), prisms from
 ligroin, m. 144°. Refluxing 5 g. II and 6.5 g. Et2N(CH2)3CHMeNH2
 in 75 cc. C6H6, and removing the C6H6 and excess base with steam gives in
 almost quant. yield the 4-(5-diethylamino-2-pentylamino) analog, needles,
 b9 280°, m. 144° (from ligroin); picrate, needles from EtOH,
 m. 180°. II (0.01 mol.), refluxed with 0.03 atom Na in 40 cc. MeOH
 for 0.5 hr. and poured into H2O, yields almost quantitatively the 4-MeO
 analog, colorless prisms from ligroin, m. 116°. Similarly, 0.01
 mol. II, 0.03 atom Na, and 12 g. PhOH in 20 cc. dioxane give the 4-PhO
 analog, colorless prisms from ligroin, m. 141°. The following
 2-furyl-4-arylamino-6-methylquinazolines are obtained in almost quant.
 yield by refluxing 0.01 mol. II with 0.02 mol. of the corresponding
 arylamine in 40 ml. C6H6, making alkaline with Na2CO3, and removing the
 solvent and excess amine with steam: PhNH, needles from aqueous EtOH, m.
 180°; MeC6H4NH, needles from EtOH, m. 140°; p-MeOC6H4NH,
 needles from ligroin, m. 156°; p-EtOC6H4NH, silky needles from
 MeOH, m. 126°.
 IT 860191-75-9P, Quinazoline, 4-(anisidino)-2-(2-furyl)-6-methyl-
 RL: PREP (Preparation)
 (preparation of)
 RN 860191-75-9 HCPLUS
 CN Quinazoline, 4-(anisidino)-2-(2-furyl)-6-methyl- (5CI) (CA INDEX NAME)



L6 ANSWER 304 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1951:8788 HCPLUS

DOCUMENT NUMBER: 45:8788

ORIGINAL REFERENCE NO.: 45:1600f-i,1601a-c

TITLE: Furylquinazolines. I. 4-Substituted
2-furylquinazolines

AUTHOR(S): Andrisano, Renato; Modena, G.

CORPORATE SOURCE: Univ. Bologna, Italy

SOURCE: Gazzetta Chimica Italiana (1950), 80, 228-33

CODEN: GCITA9; ISSN: 0016-5603

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. following abstract In view of the plasmocidal action of quinazoline derivs. containing a pentylamine side chain (cf. Endicott, et al., C.A. 40, 5748.3; Price, et al., C.A. 40, 5747.4), some 2-furylquinazoline derivs. were prepared to study their anti-malarial activity and the comparative influence on their pharmacol. properties of the Ph and furan ring in the quinazoline nucleus. α -H₂NC₆H₄CO₂Me (20 g.) and 20 g. OC₄H₃C(:NH)OEt [cf. Ber. 25, 1416(1892)], heated 3 hrs. at 210-20°, taken up in MeOH, filtered, and the residue purified by EtOH, yields 74% of 2-furyl-4-hydroxyquinazoline (I), m. 220°. Also, 10.3 g. α -H₂NC₆H₄CO₂H and 9.5 g. OC₄H₃C(:S)NH₂ [Hantzsch, Ber. 25, 1314(1892)], heated at 150° until no more H₂S is evolved, and the product treated as before, yield approx. 74% I. I (10 g.) in 80 cc. POC₁₃ and 14 g. PCl₅, heated 100 min. (no temperature given), distilled in vacuo, the residue neutralized with NH₄OH, mixed with ice water, and the crystallized product dried and extracted with C₆H₆, yield 9 g. (80%) of 2-furyl-4-chloroquinazoline (II). Hydrolysis by 5% alc. KOH yields I. II (4.1 g.) and 5 g. H₂NCHMe(CH₂)₃NET₂ in 60 cc. C₆H₆, refluxed 3 hrs., made alkaline with Na₂CO₃, and steam-distilled, leave a pasty residue which could

not

be crystallized even after distillation in vacuo (b16 286°). However, with alc. picric acid it formed, after purification by EtOH, a dipicrate, C₃₃H₃₄O₁₅N₁₀, m. 179°, and with H₃PO₄ a monohydrated diphosphate, C₂₁H₃₆O₁₀N₄P₂, m. 210°. The wts. of these corresponded to an almost 100% yield of 2-furyl-4-(4-diethylamino-1-methylbutylamino)quinazoline (III). III is also formed by the same procedure, but in the presence of PhOH without solvent. II (0.01 mol.) and alc. NaOMe (from 0.03 atom Na in 40 cc. MeOH), refluxed 1 hr., diluted with water, extracted with Et₂O, the extract evaporated, and the oil residue distilled

in vacuo (b16 212°), give, after purification by ligroin, a good yield of 2-furyl-4-methoxyquinazoline, m. 65°. II (0.01 mol.) and NaOPh (from 0.03 atom Na, 12 g. PhOH, and 20 cc. dioxane), refluxed 1 hr.,

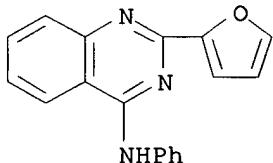
poured into water, and NaOH added, give, after purification by ligroin, almost 100% of 2-furyl-4-phenoxyquinazoline (IV), m. 135°. Alc. II, treated while refluxing with anhydrous NH₃ for 1 hr., diluted with water, and the precipitate purified by EtOH, yields almost 100% 2-furyl-4-aminoquinazoline, m. 225°. II (0.01 mol.) in C₆H₆ and 0.02 mol. of arylamine in 40 cc. C₆H₆, refluxed 1 hr., made alkaline with Na₂CO₃, steam-distilled, and the residues purified by EtOH, yielded almost 100% of the following 2-furyl-4-(arylarnino)quinazolines: NHPH, m. 115°; NHC₆H₄Me, m. 133°; NHC₆H₄OMe, m. 110°; NHC₆H₄OEt, m. 105°. The extreme reactivity of the Cl in II is similar to the behavior of Cl in 2,4,1-(O₂N)C₁₀H₅Cl (cf. Mangini and Frenguelli, C.A. 32, 1258.3) and the Cl in 4-chloroquinazoline (cf. Tomisek and Christensen, C.A. 32, 1259.1). This is in harmony with the theory of Bonino and the expts. of Mangini and Frenguelli (Atti accad. sci. Bologna [10] 1, 201(1944); C.A. 33, 5398.6), and of the pharmacol. expts. of Erlenmeyer (C.A. 41, 1671g) concerning the analogy between the heterocyclic N atom and the aromatic CNO₂ group, which, by strongly polarizing the electronic cloud in relation to the nuclear CCl group, increase the tendency toward replacement of the Cl.

IT 157863-04-2P, Quinazoline, 4-anilino-2-(2-furyl)-

RL: PREP (Preparation)
(preparation of)

RN 157863-04-2 HCPLUS

CN 4-Quinazolinamine, 2-(2-furanyl)-N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 305 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1950:56393 HCPLUS

DOCUMENT NUMBER: 44:56393

ORIGINAL REFERENCE NO.: 44:10716b-i

TITLE: Chemistry of simple heterocyclic systems. V. A comparative study of some 4-substituted cinnolines, quinazolines, and quinolines

AUTHOR(S): Keneford, J. R.; Morley, J. S.; Simpson, J. C. E.; Wright, P. H.

CORPORATE SOURCE: Liverpool School of Trop. Med., UK

SOURCE: Journal of the Chemical Society (1950) 1104-11

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 44:56393

AB cf. C.A. 44, 7844b. An account is given of the reactions undergone by derivs. of cinnoline (I), quinazoline (II), and quinoline (III) containing a series of identical substituents attached to C-4; these include the hydrolysis of 4-NH₂, 4-Cl, and 4-PhO derivs. of I-III and the reaction of the 4-Cl derivs. with PhOK and the amination of the 4-PhO derivs.

6-Nitro-4-aminocinnoline (3.3 g.) in 40 cc. AcOH, added to 14.8 g. SnCl₂ in 32 cc. concentrated HCl and 11 cc. H₂O, gives 80% 4,6-diaminocinnoline, gray,

m. 260° (decomposition); HCl salt, with 0.75 mol. H₂O, orange, m.

315-16° (decomposition); di-Ac derivative, with 1 mol. H₂O, m. 272-3° (decomposition). 6-Chloro-4-acetoxycinnoline, m. 159-60°, 90-5%.

6-Nitro-4-hydroxycinnoline (IV) (10 g.) in 175 cc. 2% aqueous KOH, treated at 50° with 5 cc. Me₂SO₄, gives 55% of the Me nitronate (V), m. 223-5° (decomposition); the alc. mother liquors yield 4.8% 6-nitro-1-methyl-4(1H)-cinnolone, m. 190-1°; 2 g. IV and 2.5 g. p-MeCr₆H₄SO₃Me, heated 2 h. at 150°, give 0.7 g. V.

6-Nitro-4-hydroxy-3-methylcinnoline (1 g.) in 21 cc. 2% aqueous KOH at 45°, treated with 0.5 cc. Me₂SO₄, gives 0.31 g.

6-nitro-1,3-dimethyl-4(1H)-cinnolone, yellow, m. 181-3°, and 0.15 g. of the Me nitronate (VI), orange, m. 161-2°; if the quantity of alkali is increased slightly, the yield of VI is reduced, and with 50 cc. alkali no III could be isolated. 4-Chloro-6-nitro-3-methylcinnoline and MeONa in MeOH give 6-nitro-4-methoxy-3-methylcinnoline, golden, m. 149-50°; it is rapidly hydrolyzed by dilute mineral acid. 5(or 7)-Nitro-4-hydroxy-8-methylcinnoline and Me₂SO₄ give 5(or 7)-nitro-1,8-dimethyl-4(1H)-cinnolone, beige, m. 257-8° (decomposition).

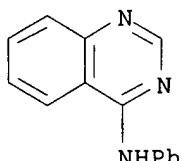
8-Nitro-4-hydroxyquinoline (200 mg.) in 1 cc. Ac₂O, refluxed 6 h., gives 120 mg. of the Ac derivative, m. 142-3°; 4-hydroxy- and 6-nitro-4-hydroxyquinolines were quant. recovered unchanged. The phenoxylation of 4-chlorocinnoline is complete after 1 h. at 95°; 4-phenoxyquinoline is obtained in 95% yield after 1 h. at 125-30°. The 4-PhO derivs. of I-II (2 g.) and 12 g. AcONH₄ show complete reaction in 9 min. at 195° and that of III in 15 min. 4-Chloroquinazoline (2 g.) and 0.14 g. MeONa in 6 cc. MeOH give, after 5 min., 0.16 g. of the 4-MeO analog; 4-chlorocinnoline after 1 h. gives 0.08 g. of the MeO compound; 4-chloroquinoline, refluxed 6 h., gives 90% unchanged material; 2.2 g. and 0.8 g. MeONa, heated 3 h. at 140°, give 1.95 g. of the MeO compound. By condensing the 4-Cl derivs. with PhNH₂ in weakly acid aqueous Me₂CO, 4-anilino derivs. of each heterocyclic type can be prepared rapidly and in good yield. The differences in reactivity between derivs. of I-III are considered in relation to their strengths as acids or bases. There is substantial qual. agreement between the observed order of reactivity of comparable compds. of each type and the predicted order as deduced from the electron d. calcns. of Longuet-Higgins and Coulson (C.A. 44, 387i).

IT 34923-95-0P, Quinazoline, 4-anilino-

RL: PREP (Preparation)
(preparation of)

RN 34923-95-0 HCAPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 306 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1950:40787 HCAPLUS

DOCUMENT NUMBER: 44:40787

ORIGINAL REFERENCE NO.: 44:7844a-e

TITLE: Chemistry of simple heterocyclic systems. IV. Basic strengths of some 4-substituted cinnolines, quinazolines, and quinolines

AUTHOR(S): Keneford, J. R.; Morley, J. S.; Simpson, J. C. E.; Wright, P. H.

CORPORATE SOURCE: School Tropical Med., Liverpool, UK

SOURCE: Journal of the Chemical Society (1949) 1356-8

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE:

Journal

LANGUAGE:

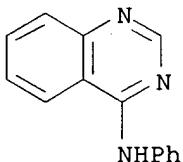
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AB cf. C.A. 44, 636e. Potentiometric detns. gave the basic strengths in 50% aqueous EtOH at 21-2° (concentration in mols./l. + 103) (cf. Pouterman and Girardet, C.A. 41,4493i; Elderfield, et al., C.A. 41, 5529c). Quinoline (I), Quinazoline (II), Cinnoline (III); pKa, c, pKa, c, pKa, c; 4-HO, 2.41, 4.96, 2.07, 4.93, 1.77, 4.93; 4-Cl, 2.59, 5.26, 2.10, 5.62, 2.08, 5.47; 4-PhO, 4.42, 5.16, 2.44, 4.08, 2.27, 4.05; H, 5.0, ..., 2.49, 3.62, 2.51, 14.59; 2.51, 6.18; 2.51, 4.96; 4-MeO, 5.35, 5.16, 2.73, 6.61, 2.71, 3.62; 6,4-O2N(H2N), 6.41, 4.45, 3.71, 2.94, 5.08, 3.60; 4-PhNH, 7.52, 5.00, 4.65, 5.00, 5.31, 5.00; 4-NH2, 8.47, 6.58, 5.17, 6.44, 6.26, 4.72; The following detns. at 25°. 4,6-Cl(O2N), 2.13, 3.66, ..., ..., ..., ..., ..., 4,8-Cl(O2N), 2.64, 3.90, ..., ..., ..., ..., 8,4-O2N(PhO), 2.94, 2.10, ..., 2.49, 2.07; 6,4-O2N(PhO), 3.25, 2.09, ..., 3.15, 2.14; 8,4-O2N(H2N), 6.63, 3.92, ..., ..., ..., 4,6-(NH2)2, ..., ..., ..., 6.86, 4.10; The acid strengths of the 4-OH derivs. were: I, pKa 12.43, c 6.21; II, 9.98, 6.16; III, 9.53, 6.16. For the H, OH, Cl, OPh, and OMe derivs. the order of basicity was I > II > III. However, for the NH2 and RNH derivs. the order was I > III > II, probably owing to abnormally low values for II. Among the latter derivs. only those of II were hydrolyzed to OH derivs. in acid solution

IT 34923-95-0, Quinazoline, 4-anilino-
(basic strength of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 307 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1950:3125 HCPLUS

DOCUMENT NUMBER: 44:3125

ORIGINAL REFERENCE NO.: 44:635h-i,636a-e

TITLE: Chemistry of simple heterocyclic systems. II.
Condensation of 4-chloro-6- and 7-nitroquinazoline
with amines

AUTHOR(S): Morley, J. S.; Simpson, J. C. E.

SOURCE: Journal of the Chemical Society (1949) 1014-17

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 43, 3420c. The condensation of 4-chloro-6-(I) and -7-nitroquinazoline (II) with a variety of primary aromatic and heterocyclic amines has been studied and the results have been correlated with the basic strength and nature of the amines. I and II do not condense with primary heterocyclic amines in which a prototropic change to an iminodihydro derivative is formally possible; condensation occurs between I and II and aromatic amines or bz-heterocyclic amines provided that the pKa values of such amines lie within the approx. range 1-5.2. Condensation does not occur if the pKa values of the amines lie on either side of this range. These results accord with the view that the reaction between chloro-heterocyclic compds. and amines is acid catalyzed. I and II did not react with 2,4-(O2N)2C6H3NH2, 1,2-O2NC10H6NH2, PhCH2NH2, 4-aminoquinazoline and its 6-NO2 derivative, 4-aminocinnoline and the 6-Cl and

6-NO₂ derivs., 6-nitro-4-aminoquinazoline, and 2-aminoquinoline. In nearly all these cases, the nonoccurrence of condensation was demonstrated by the isolation of the chloro- or hydroxyquinazoline and sometimes of the amine also. The following compds. were prepared from I or II and 5-10% excess of the appropriate amine in 50% aqueous Me₂CO containing 2-3 drops concentrated

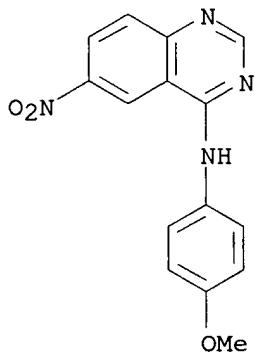
HCl by refluxing 0.5 hrs. 6-Nitro-4-(m-nitroanilino)quinazoline (III), yellow, m. 270-1°, 85%; 7-NO₂ isomer, with 0.5 mol. H₂O, pale yellow, m. 284-5°, 83%; 4-(p-nitroanilino) isomer of III, bright yellow, m. 319-20° (decomposition), 98%; 7-NO₂ isomer, yellow, m. 291-2° (decomposition), 95%; 6-nitro-4-(6-methyl-3-quinolylamino)quinazoline, deep yellow, m. 294-5°, 100%; 7-NO₂ isomer, bright yellow, m. 337-8° (decomposition), 100%; 7-nitro-4-(4-amino-2,6-dihydroxy-5-pyrimidylamino)quinazoline, with 0.5 mol. H₂O, orange, does not m. at 340°, 81%; the 6-NO₂ isomer, pale orange, does not m. at 340°, was not purified; 6-nitro-4-p-anisidinoquinazoline, orange needles (from aqueous EtOH), or bright red prisms (absolute EtOH), m. 203-5°, 100%; 7-NO₂ isomer, maroon, m. 236-8°, 100%; 6-nitro-4-(5-quinolylamino)quinazoline, buff, m. 282-3° (decomposition) 96%; 7-NO₂ isomer, yellow, m. 301-2° (decomposition), 95%; 6-nitro-4-(6-quinolylamino) quinazoline, yellow, m. 333-5° (decomposition), 83%; 7-NO₂ isomer, as the di-HCl salt with 1 mol. H₂O, pale yellow, m. 319-20° (decomposition). A characteristic reaction of the arylaminoquinazolines was the production of a deep red color on treatment with dilute aqueous-alc. alkali.

IT 860191-71-5P, Quinazoline, 4-p-anisidino-6-nitro-

RL: PREP (Preparation)
(preparation of)

RN 860191-71-5 HCPLUS

CN Quinazoline, 4-p-anisidino-6-nitro- (5CI) (CA INDEX NAME)



L6 ANSWER 308 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1949:15090 HCPLUS

DOCUMENT NUMBER: 43:15090

ORIGINAL REFERENCE NO.: 43:2952b-i,2953a-c

TITLE: Synthetic antimalarials. XXXII. Some 4-arylaminoo- and 4-arylhthio-2-(aminoalkylamino)quinazolines and 2-arylhthio-4-(aminoalkylamino)quinazolines

AUTHOR(S): Curd, F. H. S.; Hoggarth, E.; Landquist, J. K.; Rose, F. L.

SOURCE: Journal of the Chemical Society (1948) 1766-73
CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB 2-Chloro-4-hydroxyquinazoline (6.1 g.) and 5 cc. Et₂NC₂H₄NH₂, heated 1 hr.

at 140°, give 2-(2-diethylaminoethylamino)-4-hydroxyquinazoline (I), b0.001 188-95° (bath temperature), glass with indefinite m.p. (hydrate m. 96-8°); (3-diethylaminopropylamino) homolog b0.001 185-90° (bath) (hydrate m. 96-7°); [3-(1-piperidyl)propylamino] analog, with 0.5 mol. H₂O, m. 117-19°; (3-dibutylaminopropylamino) analog, with 0.5 mol. H₂O, pale yellow, m. 103-4°. I (8.1 g.) and 25 cc. POC₁₃, refluxed 1 hr., give 4-chloro-2-(2-diethylaminoethylamino)quinazoline (II), b0.001 170-5° (bath) (sesquipicrate, yellow, m. 205°); (3-diethylaminopropylamino) homolog, yellow, b0.2 210-12°; [3-(1-piperidyl)propylamino] analog b0.15 190-5°, m. 71°; (3-dibutylaminopropylamino) compound (sesquipicrate m. 157-9°).

2,4-Dichloroquinazoline (20 g.) and 12 g. p-ClC₆H₄NH₂, stirred 48 hrs. at room temperature with 14 g. AcONa in 400 cc. H₂O, give 2-chloro-4-p-chloroanilinoquinazoline (III), m. 210-15°. II (5.8 g.) and 5 g. p-ClC₆H₄NH₂, heated 2 hrs. at 130-40°, give 6 g. of the oily 4-p-chloroanilino-2-(2-diethylaminoethylamino)quinazoline (IV), whose di-HCl salt m. 262-3° and dipicrate, yellow, m. 232-3°; 2-(3-diethylaminopropylamino) homolog, m. 107-8°; 2-[3-(1-piperidyl)propylamino] compound, m. 129° (di-HCl salt m. 238-40°; picrate, yellow, m. 228-9°; acetate, with 1 mol. H₂O, m. 114-15°); 2-(3-dibutylaminopropylamino) analog-2HCl, with 1 mol. H₂O, m. 125-6°. 4-p-Methoxyanilino-2-(3-diethylaminopropylamino)quinazoline-2HCl m. 228-30°. II (4.5 g.) and 4.5 g. p-ClC₆H₄SH, heated to 130°, give 2.1 g.

2-(2-diethylaminoethylamino)-4-(p-chlorophenylmercapto)quinazoline (IVA), yellow, m. 92°; (3-diethylaminopropylamino) homolog, pale yellow, m. 100°. 2-Chloro-4-(3-diethylaminopropylamino)quinazoline-H₂O (15 g.) and 15 g. p-ClC₆H₄SH, heated 3 hrs. at 120-30°, give 12 g.

4-(3-diethylaminopropylamino)-4-(p-chlorophenylmercapto)quinazoline, m. 96°; 2-(p-tolylmercapto) analog m. 121°.

4-(2-Diethylaminoethylamino)-2-(p-chlorophenylmercapto)quinazoline (VA) m. 123°. 2-Chloro-4-(2-diethylaminoethylamino)quinazoline hydrate (5.6 g.) and 2.5 cc. Et₂NC₂H₄NH₂, heated 2 hrs. at 130°, give 2.8 g. 2,4-bis(2-diethylaminoethylamino)quinazoline (VI), pale yellow, b0.1 230-2° (tripicrate m. 193-4° and 213-14°; the higher-melting form results from the other on standing in contact with the solution; tri-HCl salt, with 1 mol. H₂O, m. 191-2°). III (6 g.) and 5 cc. Et₂NC₂H₄NH₂, heated 3.5 hrs. at 120-30°, give p-ClC₆H₄NH₂, VI, and IV. 2,4-Dichloroquinazoline (8 g.) and p-ClC₆H₄SH in 100 cc. dry ether, shaken 4 hrs. and kept overnight, give 2-chloro-4-(p-chlorophenylmercapto)quinazoline (VIA), m. 156-7°.

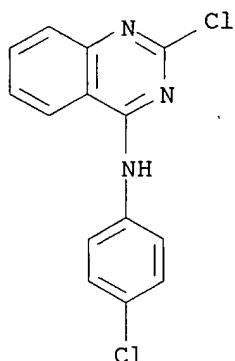
2-Chloro-4-hydroxyquinazoline (3.6 g.) and 2.9 g. p-ClC₆H₄SH, heated at 100°, give 5.2 g. 4-hydroxy-2-(p-chlorophenylmercapto)quinazoline (VII), m. 246°; crystallization from EtOC₂H₄OH gives 2,4-dihydroxyquinazoline. VII (3 g.) and 15 cc. POC₁₃, refluxed 15 min., give 1.8 g. 4-chloro-2-(p-chlorophenylmercapto)quinazoline (VIII), m. 126°. VIA (3.1 g.) and 1.5 g. p-ClC₆H₄SH, heated at 100° and the powdered melt heated 1 hr. at 100°, give 3.3 g.

2,4-bis(p-chlorophenylmercapto)quinazoline (IX), m. 134-5°; this results also from VIII. VIII (1 g.) and 0.5 g. Et₂NC₂H₄NH₂ in 15 cc. EtOH, boiled 2 hrs., give 0.8 g. VA; VIA gives a mixture of VA and IX. Et₂N(CH₂)₃NH₂ reacts similarly. IX (2.1 g.) and 0.6 g. Et₂NC₂H₄NH₂ in 25 cc. EtOH and 10 cc. EtOC₂H₄OH, heated 6 hrs. on the steam bath, give 0.5 g. p-ClC₆H₄SH, 0.4 g. unchanged IX, and 1.3 g. VA. IVA (1.6 g.), 1.2 cc. Et₂NC₂H₄NH₂, and 10 cc. EtOH, refluxed 4 hrs., give 0.25 g. p-ClC₆H₄SH and VI; VA was unchanged under similar conditions. VIA (3.1 g.) and 0.4 g. NaOH in 25 cc. EtOH and 10 cc. H₂O, refluxed 4 hrs., give 0.9 g. IX. VA or VI does not react with p-ClC₆H₄SH in EtOH (refluxing 10 hrs.).

2,4-Bis(p-chloroanilino)quinazoline-HCl and Et₂NC₂H₄NH₂, heated 3 hrs. at 130-40°, give 2-(p-chloroanilino)-4-(2-

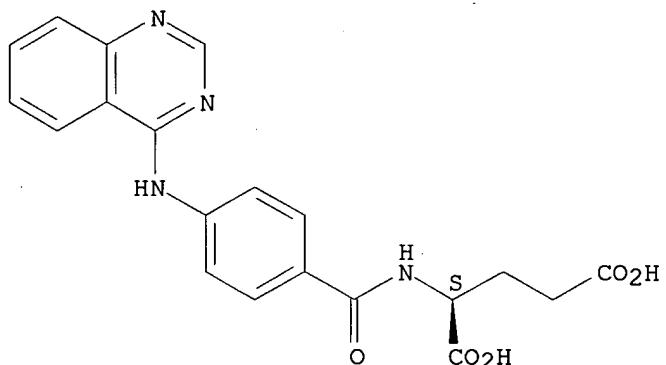
diethylaminoethylamino)quinazoline-2HCl; this results also from 2-(p-chloroanilino)-4-(2-hydroxyethylamino)quinazoline-HCl. It seems possible that these displacements of 4-aryl- and 4-alkylamino residues may involve dissociation of a quinazolinium ion, followed by recombination with a different amine.

- IT 174074-90-9P, Quinazoline, 2-chloro-4-p-chloroanilino-
 RL: PREP (Preparation)
 (preparation of)
- RN 174074-90-9 HCPLUS
- CN 4-Quinazolinamine, 2-chloro-N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



- L6 ANSWER 309 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1949:9130 HCPLUS
 DOCUMENT NUMBER: 43:9130
 ORIGINAL REFERENCE NO.: 43:1914b-c
 TITLE: N-[4-(4-Quinazolylamino) benzoyl] glutamic acid
 INVENTOR(S): Avakian, Souren; Martin, Gustav J.
 PATENT ASSIGNEE(S): National Drug Co.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
- | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|---|----------|-----------------|------|
| US 2440649 | | 19480427 | US | |
| AB | 4-Chloroquinazoline and N-(p-aminobenzoyl)glutamic acid in alc. are refluxed to yield the product, m. 240-2°, which has biol. properties like folic acid. | | | |
| IT | 884312-30-5P, Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)-
RL: PREP (Preparation)
(preparation of) | | | |
| RN | 884312-30-5 HCPLUS | | | |
| CN | Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)- (5CI) (CA INDEX NAME) | | | |

Absolute stereochemistry.



L6 ANSWER 310 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1948:36558 HCAPLUS

DOCUMENT NUMBER: 42:36558

ORIGINAL REFERENCE NO.: 42:7781d-h

TITLE: Quinazolines. VI. Syntheses of certain
2-methyl-4-substituted quinazolines

AUTHOR(S): Tomisek, Arthur J.; Christensen, Bert E.

CORPORATE SOURCE: Oregon State Coll., Corvallis

SOURCE: Journal of the American Chemical Society (1948), 70,
2423-5

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 42, 6367f. 5,2-Cl(H₂N)C₆H₃CO₂H (25 g.) and 75 ml. Ac₂O, refluxed
1 hr., give 21.8 g. 6-chloro-2-methyl-3,1,4H-benzoxaz-4-one, m.
124-5° (m.p.s. corrected); concentrated NH₄OH (4 hrs.) yields
N-acetyl-5-chloroanthranilamide, m. 183°; without isolation of the
amide, the solution is heated several min. with 10 ml. 10% NaOH, the product
dissolved by addition of excess hot 10% NaOH, and the solution adjusted to pH
8;

there results 10.45% (37% over-all yield) 6-chloro-2-methyl-4(3H)-
quinazolone (I), m. 287°, and (from the filtrate) 5.4 g.
N-acetyl-5-chloroanthranilic acid, m. 204°. 2-Methyl-4(3H)-
quinazolone (16 g.) and 21.6 g. P₂S₅, mixed dry and then refluxed 2 hrs.
with 100 ml. xylene, give 49% 2-methyl-4-mercaptopquinazoline (II), m.
217-19°. Similarly I yields 55% of the 6-Cl derivative (III) of II,
yellow, m. 276-8° (decomposition). II (1.47 g.) and 5 ml. HOCH₂CH₂NH₂,
heated 7 hrs. at 80°, yield 88% 4-(2-hydroxyethylamino)-2-
methylquinazoline, yellow prisms and spherulites, m. 164-6°,
resolidifies to needles, m. 174.5-6°. III (1.75 g.) and 4 g.
p-MeOC₆H₄NH₂, heated 6 hrs. at 190°, give 0.59 g.
6-chloro-4-p-methoxyanilino-2-methylquinazoline, whose HCl salt, yellow,
m. 321° (decomposition) (capillary block preheated to 319°).
2,4-Dimethylquinazoline (2.5 g.) in 20 ml. concentrated H₂SO₄, treated with 10
ml. fuming HNO₃, 1 hr. at 75°, gives 1.84 g. 2-methyl-6-nitro-4(3H)-
quinazolone, m. 302-4° (decomposition); this results in 2.8-g. yield
from 2.5 g. 2-methyl-4-(3H)-quinazolone; it does not react with P₂S₅
(boiling 12 hrs. in p-cymene).

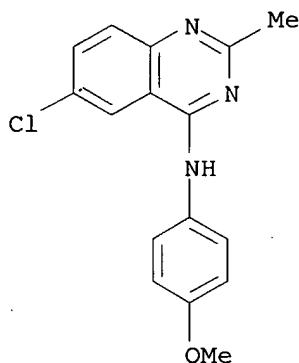
IT 7505-85-3P, Quinazoline, 4-p-anisidino-6-chloro-2-methyl-,
hydrochloride

RL: PREP (Preparation)
(preparation of)

RN 7505-85-3 HCAPLUS

CN Quinazoline, 4-p-anisidino-6-chloro-2-methyl-, monohydrochloride (8CI)

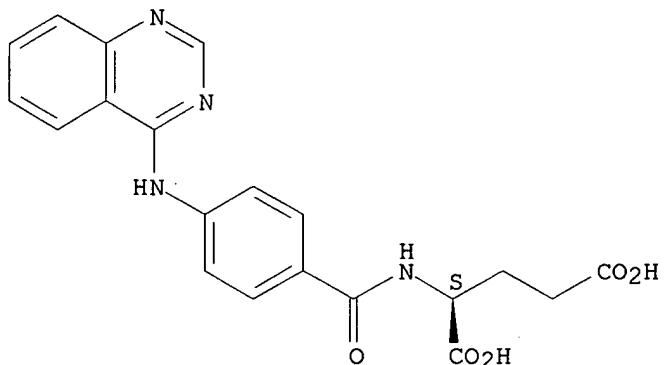
(CA INDEX NAME)



● HCl

L6 ANSWER 311 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1948:23557 HCPLUS
 DOCUMENT NUMBER: 42:23557
 ORIGINAL REFERENCE NO.: 42:5093f-h
 TITLE: Further observations on the specificity of the folic acid molecule
 AUTHOR(S): Spies, Tom D.; Lopez, Guillermo Garcia; Stone, Robert E.; Milanes, Fernando; Brandenberg, Robert O.; Aramburu, Tomas
 CORPORATE SOURCE: Hillman Hosp., Birmingham, AL
 SOURCE: Blood (1948), 3, 121-6
 CODEN: BLOOAW; ISSN: 0006-4971
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 41, 7460h. Methylfolic acid, N-[4-(4-quinazolylamino)benzoyl]glutamic acid, the Mg salt of formylpteroylglutamic acid, the Mg salt of formylpteroic acid, pteroylaspartic acid, hydroxyfolic acid, and hydroxypteroic acid were studied. Only the Mg salt of formylpteroylglutamic acid was effective in producing reticulocytosis and increases in the number of red and white blood cells, platelets, and hemoglobin. Per unit of weight, it was less effective than folic acid.
 IT 884312-30-5P, Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)-
 RL: PREP (Preparation)
 (preparation of)
 RN 884312-30-5 HCPLUS
 CN Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)- (5CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 312 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1948:23284 HCAPLUS

DOCUMENT NUMBER: 42:23284

ORIGINAL REFERENCE NO.: 42:5028d-i,5029a-f

TITLE: Simple heterocyclic systems. I. Reactions of 6- and 7-nitro-4-hydroxyquinazoline and their derivatives

AUTHOR(S): Morley, J. S.; Simpson, J. C. E.

CORPORATE SOURCE: Liverpool School of Trop. Med., UK

SOURCE: Journal of the Chemical Society (1948) 360-6

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB The reactions of 6- (I) and 7-nitro-4-hydroxyquinazolines (II) are compared with those of 6-nitro-4-hydroxycinnoline (III). I and II fail to react with Ac₂O under conditions which result in the quant. acetylation of III; replacement of the HO group by Cl also occurs less readily with I and II than with III. I and II have slightly basic properties in addition to their acidic nature, whereas III is devoid of basic character. In addition, the reaction with Me₂SO₄ is markedly different. The crude Cl compound (IV) from 10 g. I and 6 g. KOH in 60 g. PhOH, heated 1 h. at 90-5°, gives 6.1 g. 6-nitro-4-phenoxyquinazoline (V), m. 148-9°; 7-NO₂ isomer (VI) (14.7 g. from 15 g. II), m. 173.5-4°. Crude IV (from 20 g. I), added to 80 g. PhOH and 40 g. (NH₄)₂CO₃, the mixture heated 1 h. at 90-5°, diluted with H₂O, excess NaOH added, and the product (20.2 g.) added to 100 g. fused AcONH₄ and heated 0.25 h. at 180°, gives 77% 6-nitro-4-aminoquinazoline (VII), lemon-yellow, m. 320-30.5° Ac derivative (VIII), pale yellow, m. 262-3° (decomposition); 1 g. pure IV and 20 cc. NH₄OH (d. 0.88), kept 4 days at room temperature, give 70 mg. IV and 0.76

g. VIII. The crude Cl derivative (IX) (from 20 g. II) yields 15.5 g. of a mixture (X) m. 265-70°; fusion with 77 g. AcONH₄ gives 69% 7-nitro-4-aminoquinazoline (XI), pale yellow, m. 303-5°. Extraction of 5.6 g. X with boiling EtOH gives 1.7 g. VI and 1 g. XI. Pure IX (1 g.) with NH₄OH gives 0.49 g. IX and 0.37 g. XI. The Ac derivative of XI, pale yellow, m. 240-2° (decomposition). Pure IV (2 g.) and 0.6 g. MeONa in 50 cc. MeOH, refluxed 0.5 h., yield 75% 6-nitro-4-methoxyquinazoline, yellow, m. 118-19°; 7-NO₂ isomer, m. 137-8°. Crude IV (from 10 g. I), 5 cc. PhNH₂, 0.5 cc. concentrated HCl, and 100 cc. 50% aqueous Me₂CO, refluxed 0.5 h., give 80% (based on I) 6-nitro-4-anilinoquinazoline (XII), yellow, m. 236-7.5° (decomposition); 10 g. XII and 7.7 g. p-MeC₆H₄SO₃Me, heated 30 min. at 148-50°, the cold mass digested with 100 cc. hot EtOH, and the product crystallized from hot H₂O, give 85% 6-nitro-4-anilino-1-methylquinazolinium p-toluenesulfonate (XIII), deep yellow, m. 249-50° (decomposition); KI gives 88% of the iodide (XIV), yellow, m.

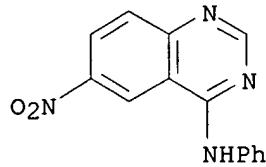
247-8° (decomposition); occasionally a 2nd form, m. 254-6° (decomposition), was observed; 1 g. XIV in 60 cc. H₂O at 91-3°, reduced with 1.25 g. Fe (added during 0.5 h., with stirring for an addnl. hr.), gives 89% 6-amino-4-anilino-1-methylquinazolinium iodide (XV), golden, m. 287-8°. The 7-NO₂ isomer of XII, yellow, m. 251-2° (decomposition), 70%; the 7-NO₂ isomer of XIII, yellow, m. 257-8° (decomposition), 92%; that of XIV, orange, m. 256-7° (decomposition), 93%; that of XV, brownish yellow, m. 266-8°, 90%. 6-Nitro-3-methyl-4(3H)-quinazolone (XVI) (prepared in 75% yield from I and Me₂SO₄ in 2% aqueous KOH), refluxed 0.5 h. with 2 N NaOH, gives 95.4% MeNH₂ and 5,2-O₂N(H₂N)C₆H₃CO₂H. VIII (5 g.) and 4.2 g. p-MeC₆H₄SO₃Me, heated 10 min. at 160°, the cooled mass extracted with 100 cc. hot H₂O, and the extract heated 0.75 h. with 50 cc. concentrated HCl, give 1.9 g. 6-nitro-1-methyl-4-(1H)-quinazolone (XVII), m. 272-3°; 1 g. V and 0.7 g. p-MeC₆H₄SO₃Me, heated at 125°, give 1 g. of the p-toluenesulfonate of XVII, with 1 mol. H₂O, m. 234-5°; with hot H₂O, the salt yields XVII. XVII (0.2 g.) in 21 cc. hot H₂O and 5 cc. 2 N NaOH yields 0.2 g. 5-nitro-2-(methylamino)benzamide, yellow, m. 218-18.5°; if XVII is refluxed 40 min. with dilute NaOH, the product is 5,2-O₂N(MeNH)C₆H₃CO₂H (Me ester, greenish yellow, m. 146-7°). The 7-NO₂ isomer (XVIII) of XVII, with 2/3 mol. H₂O, flesh-colored, m. 215-16°; p-toluenesulfonate, with 1 mol. H₂O, m. 247-7.5°; addition of 5 cc. 2 N NaOH to 1 g. XVIII in 35 cc. hot H₂O gives 0.27 g. 4-nitro-2-(methylamino)benzamide, orange, m. 188-9°; the filtrate, acidified with H₃PO₄, yields 0.56 g. 4-nitro-2-(methylformamido)benzoic acid, yellow, m. 203-4° (decomposition); distillation of the filtrate gives HCO₂H; if the alkaline solution of XVIII is refluxed, the product is 4-nitro-2-(methylamino)benzoic acid (XIX), orange-red, m. 259-60° (decomposition). 4,2-O₂N(H₂N)C₆H₃CO₂H (5 g.) in 50 cc. C₅H₅N, treated with 7 g. p-MeC₆H₄SO₂Cl 2 days at room temperature, gives 5.8 g. Me 4-nitro-2-(p-tolylsulfonamido)benzoate, m. 183-4°; 3 g. of the dry Na salt and 12 cc. MeI, refluxed 4 h. in 60 cc. Me₂CO, give 2.75 g. Me 4-nitro-2-(N-methyl-p-tolylsulfonamido)benzoate, m. 126-8°; concentrated H₂SO₄ (0.5 h. at 80-90°) gives the Me ester of XIX, orange, m. 124-5°, hydrolysis of which with N NaOH (refluxing 0.5 h.) gives XIX. It is probable that in the 4-hydroxyquinazolines the basic center is N1 and thus does not coincide with the site of N-alkylation. The facile alkaline and acid hydrolyzes of 4-amino- to 4-hydroxyquinazolines are readily explained by the amidine mechanism, on the assumption that such compds. react in these hydrolyzes in the iminodihydro (semicyclic amidine) and not in the amine (cyclic amidine) form. I and II are not attacked under more drastic alkaline conditions. An explanation of this difference in reactivity is advanced.

IT 49675-75-4P, Quinazoline, 4-anilino-6-nitro-

RL: PREP (Preparation)
(preparation of)

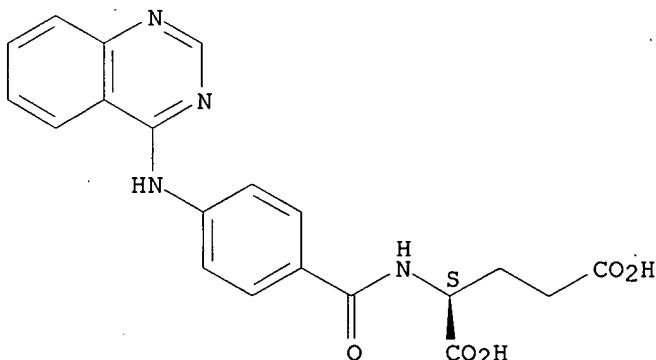
RN 49675-75-4 HCAPLUS

CN 4-Quinazolinamine, 6-nitro-N-phenyl- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 42:21491
 ORIGINAL REFERENCE NO.: 42:4617b-c
 TITLE: Effect of folic acid analogs on the action of dopa
 decarboxylase
 AUTHOR(S): Martin, Gustav J.; Beiler, J. M.
 CORPORATE SOURCE: Natl. Drug Co., Philadelphia, PA
 SOURCE: Journal of the American Pharmaceutical Association,
 Scientific Edition (1948), 37, 32-3
 CODEN: JAPMA8; ISSN: 0095-9553
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB With a previously reported method of assay (C.A. 42. 1975e) for the
 inhibiting power of folic acid analogs on the decarboxylation of
 dihydroxy-L-phenylalanine by dopa decarboxylase, the following compds,
 were tested: 7-methylpternylaspartic acid, 7-methylpteroic acid,
 2-oxyfolic acid, 2-oxypteroic acid, and N-[4-[(4-
 quinazoline)amino]benzoyl]glutamic acid. The results are discussed in
 relation to the nature of the substituents, the most effective compds.
 having a substituent on the pteridyl part of the mol.
 IT 884312-30-5P, Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)-
 RL: PREP (Preparation)
 (preparation of)
 RN 884312-30-5 HCPLUS
 CN Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)- (5CI) (CA INDEX NAME)

Absolute stereochemistry.



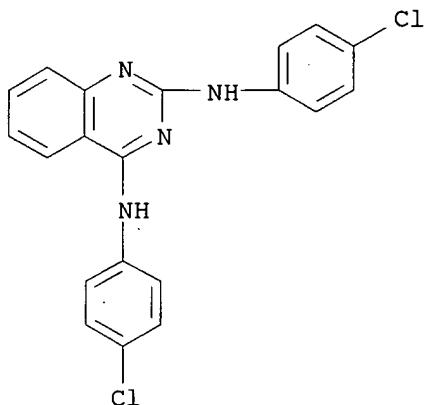
L6 ANSWER 314 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1948:786 HCPLUS
 DOCUMENT NUMBER: 42:786
 ORIGINAL REFERENCE NO.: 42:179a-i,180a-g
 TITLE: Synthetic antimalarials. XIV. Some
 2-arylamino-4-(aminoalkylamino)quinazolines
 AUTHOR(S): Curd, F. H. S.; Landquist, J. K.; Rose, F. L.
 CORPORATE SOURCE: Imperial Chem. Inds. Ltd., Blackley, UK
 SOURCE: Journal of the Chemical Society (1947) 775-83
 CODEN: JCSOA9; ISSN: 0368-1769
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 41, 5137d. At the inception of this work it appeared as if
 antimalarial activity was associated with the attachment to a heterocyclic
 nucleus of an aminoalkyl group and an aryl group through linkages capable
 of forming prototropic systems with the central nucleus. The replacement
 of the pyrimidine nucleus (cf. C.A. 40, 5054.6) by other N-containing
 heterocyclic systems was an obvious development and some analogous

quinazoline derivs. are now described. The lack of interest in this type of compound probably resulted from the statement of Magidson and Golovchinskaya (C.A. 33, 4993.5) that 4-(dialkylaminoalkylamino)quinazolines, including those carrying an addnl. substituent such as (Cl, NO₂, or NH₂ in the 6-position, were devoid of antimalarial activity; this is now shown to be wrong. 2,4-Dihydroxyquinazoline (20 g.), 60 g. POCl₃, and 9 g. PhNMe₂, refluxed 5.5 hrs., give 18.6 g. 2,4-dichloroquinazoline (I), m. 116-17°; it is best purified by vacuum distillation I (4 g.) and 5.5 g. Et₂N(CH₂)₃NH₂, heated 2 hrs. at 130°, give 2,4-bis(3-diethylaminopropylamino)quinazoline, pale yellow, b₀.02 206-8° (triplicate, yellow, m. 180°). I (0.1 g.-mole), 200 cc. H₂O, and 0.1 g.-mole of the appropriate (aminoalkyl)amine, stirred at room temperature, the mixture made alkaline to Clayton yellow with 10 N NaOH and then treated with

addnl. NaOH (4-12 hrs.) to maintain the alkalinity (until 0.1 g.-mole has been added), the solution acidified (Congo red) with HCl, unreacted I removed, and the solution treated with excess NaOH, give the following 2-chloro-4-(aminoalkylamino)quinazolines in practically quant. yield; these compds. are unexpectedly stable to acid or alkaline hydrolysis: 2-dimethylaminoethylamino, m. 96-8°; 3-dimethylaminopropylamino, m. 74°; 2-diethylaminoethylamino (II), b₀.04 185°, m. 85° (hydrate, m. 80-1°; HCl salt, m. 202-3°); 3-diethylaminopropylamino (with 2 mols. H₂O), m. 66-8°; 4-diethylaminobutylamino, m. 71°; 4-diethylamino-1-methylbutylamino, b₀.08 200-3°; (2-diethylaminoethyl)methylamino, indefinite m.p.; 3-(1-piperidyl)propylamino, m. 141°; 2-acetamidoethylamino, m. 206-7°; 2-hydroxyethylamino, m. 186°. I (19.9 g.) and 150 cc. 2 N NaOH, stirred 3 hrs., give 2-chloro-4-hydroxyquinazoline (III), m. 218-20°. III (4.5 g.), 3.2 g. p-ClC₆H₄NH₂, 30 cc. H₂O, 15 cc. Me₂CO, and 0.5 cc. 10 N HCl, refluxed 1 hr. and the HCl salt (m. 277°) in hot EtOCH₂CH₂OH made alkaline with NH₄OH and poured into H₂O, give 2-p-chloroanilino-4-hydroxyquinazoline (IV), m. 280-2°; p-anisidino analog m. 262-3°. IV (7.5 g.), 30 cc. POCl₃, and 5 cc. PhNMe₂, refluxed 0.75 hr. and the solution poured into 300 g. ice and 100 cc. 32% NaOH, give 4-chloro-2-p-chloroanilinoquinazoline (V), m. 177-8°. I (3.6 g.) and 18 g. p-ClC₆H₄NH₂, heated 3 hrs. at 140°; give 2,4-bis(p-chloroanilino)quinazoline (VI), m. 185°; this results also from V. 2-Chloro-4-ethoxyquinazoline (VII) (20.85 g.) and 12.8 g. p-ClC₆H₄NH₂ in 200 cc. EtOH, refluxed 1 hr., give 23.5 g. 2-p-chloroanilino-4-ethoxyquinazoline (VIII), m. 122° (HCl salt, pale yellow, m. 175°); hydrolysis of 1 g. VIII by refluxing 5 hrs. with 5 cc. HCl and 10 cc. H₂O gives III. 2-Chloro-4-phenoxyquinazoline (6.4 g.) and 3.2 g. p-ClC₆H₄NH₂ in 30 cc. EtOH, refluxed 1 hr., give 2.5 g. 2-p-chloroanilino-4-phenoxyquinazoline (IX), m. 186-7°. VI (19.9 g.) and MeSNa (MESH passed into 40 cc. EtOH containing 2.5 g. Na and then diluted with 40 cc. EtOH), allowed to stand 16 hrs. at room temperature, give 2-chloro-4-methylmercaptoquinazoline (X), m. 122°; with p-ClC₆H₄NH₂ in EtOH (refluxed 0.5 hr.), X yields 2-p-chloroanilino-4-(methylmercapto)quinazoline (XI), m. 176°. The compds. listed below were prepared by the following general methods. (A) V (1.2 g.), 1 cc. Et₂N(CH₂)₂NH₂, and 5 cc. AcOH, heated 1.5 hrs. at 95-100°, the mixture diluted with 20 cc. H₂O, boiled, and the filtrate treated with 5 cc. HCl, give 2-p-chloroanilino-4-(2-diethylaminoethylamino)quinazoline, m. 111-12°, as the di-HCl salt (XII), with 2 mols. H₂O, m. 253-4°; the mono-Ac derivative (as di-HCl salt) m. 248-9°. (B) II (11.15 g.), 10.5 g. p-ClC₆H₄NH₂, and 20 cc. AcOH, refluxed 2 hrs., give 11.5 g. XII. Methods A and B can be modified by heating the reactants 3 hrs. at 130-40° in the absence of AcOH. (C) II (11.15 g.), 6.6 g. p-ClC₆H₄NH₂.HCl, 40 cc. H₂O, and 0.2 cc. 10 N HCl, refluxed 1 hr., give 10 g. XII. (D) VII (2.99 g.) and 2.32 g. Et₂N(CH₂)₂NH₂, heated 2 hrs. at

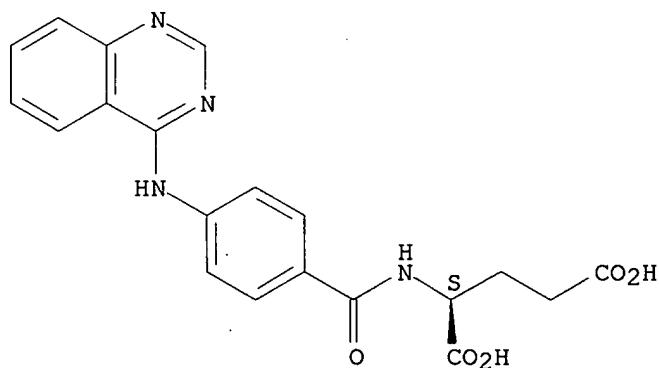
140-50°, give 4 g. XII. IX (1 g.) and 1.5 g. Et₂N(CH₂)₂NH₂, heated 2.5 hrs. at 140-50°, give 0.9 g. XII. XI (3.75 g.) and a large excess Et₂N(CH₂)₂NH₂, refluxed 6 hrs., give XII (no yield stated). 4-Substituted 2-p-chloroanilinoquinazolines: 2-aminoethylamino, m. 142° (D) (di-HCl salt, with 1.5 mols. H₂O, m. 314-16°); 6-aminohexylamino-2HCl (1 mol. H₂O), m. 261-3° (D); 2-dimethylaminoethylamino-2HCl (2.5 mols. H₂O), m. 267-8° (B, C); 3-dimethylaminopropylamino-2HCl (1.5 mols. H₂O), m. 256-8° (B); 4-dimethylaminobutylamino-2HCl (1 mol. H₂O), m. 261° (D); 5-dimethylaminoamylamino-2HCl (1.5 mols. H₂O), m. 278° (D); 6-dimethylaminohexylamino-2HCl (with 1.5 mols. H₂O), m. 156-8° and then 236° (D); 3-diethylaminopropylamino (with 0.5 mol. H₂O), m. 126-7° (A) (di-HCl salt, with 2 mols. H₂O, m. 274°); 4-diethylaminobutylamino-2HCl (with 1 mol. H₂O), m. 260-2° (B); 4-diethylamino-1-methylbutylamino-2HCl (with 2 mols. H₂O), m. 122° and then 205° (D); 3-isopropylmethylaminopropylamino-2HCl (with 2 mols. H₂O), m. 268-9° (D); 3-butylaminopropylamino-2HCl (with 1 mol. H₂O), m. 254-6° (B, D); 3-dibutylaminopropylamino-2HCl (with 0.5 mol. H₂O), m. 193-4° (D); 4-dibutylaminobutylamino-2HCl (with 2 mols. H₂O), m. 181° (D); 2-(1-pyrrolidyl)ethylamino-2HCl (with 2.5 mols. H₂O), m. 283-5° (D); 2-(1-piperidyl)ethylamino-2HCl (with 0.5 mol. H₂O), m. 276-8° (D); 3-(1-piperidyl)propylamino-2HCl (with 0.5 mol. H₂O), m. 285-6° (B, C); 2-(1-piperidyl)-1-methylethylamino-2HCl (with 3 mols. H₂O), m. 274-5° (D); 2-(1-piperidyl)-2-methylethylamino-2HCl (with 1 mol. H₂O), m. 283-6° (D); 3-[(2-diethylaminoethyl)methylamino]propylamino-3HI (with 2 mols. H₂O), m. 229° (D); methyl-(2-diethylaminoethyl)amino-2HCl (with 2 mols. H₂O), m. 76° (B); methyl(3-methylaminopropyl)amino-2HCl (with 2.5 mols. H₂O) m. 137-8° (D); 2-acetamidoethylamino, m. 183-4° (B); 2-hydroxyethylamino, m. 174° (B,D) (HCl salt, with 1 mol. H₂O, m. 286-7°). 2-Substituted derivs. of 4-(2-diethylaminoethylamino)quinazolines: 4-(methylmercapto)anilino-2HCl (with 3 mols. H₂O), m. 130-1° (B); 4-nitroanilino-2HCl (with 4 mols. H₂O), m. 286-70(C); N-ethylanilino, m. 110° (B); 2-naphthylamino, m. 126° (B); 4,8-dichloro-2-naphthylamino-2HCl (with 1 mol. H₂O), m. 284° (B); 6-bromo-2-naphthylamino-2HCl (with 2 mols. H₂O), m. 284-5° (B). 2-Substituted derivs. of 4-(3-diethylaminopropylamino)quinazolines: anilino, m. 112-14° (B); p-toluidino, m. 94° (B); p-anisidino, m. 114-15° (A, B); 2-naphthylamino, m. 141°. The results of tests against the blood-invasive forms of Plasmodium gallinaceum in chicks are given; many of the compds. show marked antimalarial activity against the endo- but no activity against the exoerythrocytic form. In this respect they resemble the 2-arylamino-4-(aminoalkylamino)-6-methylpyrimidines (C.A. 40, 5054.6) and the corresponding 5,6-disubstituted pyrimidines (C.A. 40, 5062.2) to which they are related structurally.

IT 192217-80-4P, Quinazoline, 2,4-bis(p-chloroanilino)-
 RL: PREP (Preparation)
 (preparation of)
 RN 192217-80-4 HCPLUS
 CN 2,4-Quinazolinediamine, N,N'-bis(4-chlorophenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 315 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1947:20902 HCPLUS
 DOCUMENT NUMBER: 41:20902
 ORIGINAL REFERENCE NO.: 41:4202b
 TITLE: Folic acid activity of N-[p-(4-quinazolyl)benzoyl]glutamic acid
 AUTHOR(S): Martin, Gustav J.; Moss, Jack; Avakian, Souren
 CORPORATE SOURCE: Natl. Drug Co., Philadelphia, PA
 SOURCE: Journal of Biological Chemistry (1947), 167, 737
 CODEN: JBCHA3; ISSN: 0021-9258
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB In a study seeking substitutes for folic acid, 4-chloroquinazoline was condensed with p-aminobenzoyl-1(+) -glutamic acid to produce the title compound, m. 240-2°. This was found to be a growth factor, about 0.1 to 0.01 as active as pteroylglutamic acid.
 IT 884312-30-5, Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)-, folic acid
 (activity of)
 RN 884312-30-5 HCPLUS
 CN Glutamic acid, N-(p-4-quinazolinylaminobenzoyl)- (5CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 316 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1947:20751 HCPLUS
 DOCUMENT NUMBER: 41:20751

ORIGINAL REFERENCE NO.: 41:4173i,4174a-i
 TITLE: New heterocyclic compounds
 INVENTOR(S): Curd, Francis H. S.; Landquist, Justus K.; Raison, Clifford G.; Rose, Francis L.
 PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|-------|----------|-----------------|----------|
| GB 585363 | ----- | 19470205 | GB 1944-10441 | 19440831 |
| AB New quinoline and quinazoline compds., useful as antimalarials, are prepared by the reaction of a diamine of the (di)alkylaminoalkylamine type with quinoline or quinazoline compds. containing an arylamino group in the 2-or 4-position, and a halogen, alkoxy, aryloxy, or alkyl-mercaptop group in the 4- or 2-position. The arylamino group as well as other positions of the quinoline or quinazoline may be substituted by simple nonacidic groups. The intermediate 2-arylmino-4-haloquinolines are described above. The isomeric 2-halo-4-arylaminquinolines are prepared by halogenation of the corresponding 2-OH compds. which in turn are obtained from the action of the arylamine on the 2,4-dihydroxyquinoline. The 2-arylmino-4-haloquinazolines are prepared by halogenation of the 4-OH compound, and the isomeric 2-halo-4-arylaminquinazolines by the action of the arylamine on the 2,4-dihalo compound. The 4-alkoxy, aryloxy, or alkylmercapto intermediates are prepared by the action of the appropriate alc., phenol, or mercaptan, or alkali metal derivs. thereof, on the 4-halo compds. The general procedure for the preparation of the new compds. involves refluxing the diamine and the heterocyclic intermediate for several hrs. at temps. between 120-90°; addition of aqueous NaOH to precipitate the free base; recrystn. | | | | |
| of the base, or formation of acid salts and recrystn. thereof. The following new compds. used as intermediates are described:
2-p-methoxyanilino-4-hydroxyquinazoline, m. 265-6°; these
2-p-chloroanilinoquinazolines: 4-Cl, m. 177-8°; 4-EtO, m. 122°; 4-PhO, m. 186-7°; and 4-MeS, m. 176°. From the action of the appropriate diamine on 2-p-chloroanilino-4-chloroquinazoline, the following 4-substituted derivs. of 2-p-chloroquinazoline were prepared (given is the 4-substituent and the m.p.): 2-aminoethylamino, 142° (2HCl, 314-16°); 2-acetamidoethylamino-HCl, 278-80°; 2-dimethylaminoethylamino-2-HCl, 267-8°; 2-diethylaminoethylamino-2HCl, 254-5°; 2-(1-piperidyl)ethylamino-2HCl, 280-4°; 2-(1-pyrrolidyl)-ethylamino-2HCl, 283-5°; 2-(1-piperidyl)-1-methylethylamino-2HCl, 274-5°; 3-dimethylaminopropylamino-2-HCl, 255°; 3-diethylaminopropylamino, 126-7°; 3-butylaminopropylamino-2HCl, 254-6°; 3-methylisopropylaminopropylamino-2HCl, 268-9°; 3-dibutylaminopropylamino-2HCl, 193-4°; 2-(1-piperidyl)propylamino-2HCl, 283-6°; 3-(1-piperidyl)propylamino-2HCl, 285-6°; 3-[methyl(2-diethylaminoethyl)amino]propylamino-3HI, 229°; 4-dimethylaminobutylamino-2HCl, 261°; 4-diethylaminobutylamino-2HCl, 260-2°; 4-dibutylaminobutylamino-2HCl, 181°; 4-diethylamino-1-methylbutylamino-2HCl, 122°, then solidifies and m. 250-2°; 5-dimethylaminoamylamino-2HCl, 278°; 6-aminohexylamino-2HCl, 261-3°; 6-dimethylaminohexylamino-2HCl, 156-8°, then solidifies and m. 236-8°; and methyl(3-methylaminopropyl)amino-2HCl, 137-8°, then solidifies and m. 220-50°. Similarly there were prepared 2-p-methoxyanilino-4-(3-diethylaminopropylamino)quinazoline, m. 114-15°, and 2-(3-diethylaminopropylamino)-4-p-chloroanilinoquinazoline, m. | | | | |

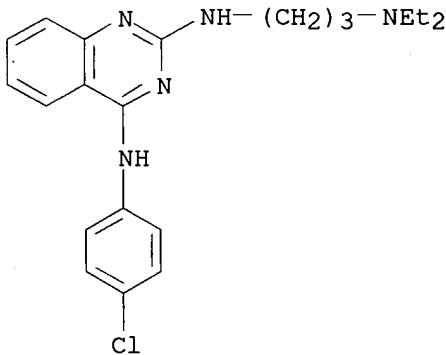
107-8°. By similar procedures were obtained the following 4-substituted derivs. of 2-p-chloroanilinoquinoline (given is the 4-substituent and the m.p.): 2-diethylaminoethylamino-2HCl, 169-71° (2HI, 252-4°); 3-dimethylaminopropylamino-2HCl, 86-8°; 3-diethylaminopropylamino, 153-5° (2HCl, 110° (decomposition)); 3-(1-piperidyl)propylamino-2HCl, 86-8°; 4-diethylaminobutylamino-2HCl, 201-3°; 4-diethylamino-1-methylbutylamino dipicrate, 230-2°. From the action of Et₂NCH₂CH₂NH₂ on other 2-arylaminoquinolines, there were obtained the following 2-substituted derivs. of 4-(2-diethylaminoethylamino)quinoline: p-toluidino, 103-5°; p-methoxyanilino-2HI, 146-8°; 2-naphthylamino-2HI, 127-8°. Similarly prepared were: 2-p-nitroanilino-4-(3-diethylaminopropylamino)quinoline-2HCl, m. 182-4°; 2-(6-bromo-2-naphthylamino)-4-(3-diethylaminopropylamino)-quinoline, m. 149-50°; 2-(2-diethylaminoethylamino)-4-p-chloroanilinoquinoline-2HI, m. 248-9°; 2-(3-dibutylaminopropylamino)-4-p-chloroanilinoquinoline-2HI, m. 200-2°; 2-p-chloroanilino-3-methyl-4-(3-diethylaminopropylamino)quinoline diperchlorate, m. 216-18°; and 2-p-chloroanilino-4-(3-diethylaminopropylamino)-7,8-benzoquinoline-2HCl, m. 108-10°. Cf. preceding abstract

IT 874497-47-9P, Quinazoline, 4-p-chloroanilino-2-(3-diethylaminopropylamino)-

RL: PREP (Preparation)
(preparation of)

RN 874497-47-9 HCAPLUS

CN Quinazoline, 4-p-chloroanilino-2-(3-diethylaminopropylamino)- (5CI) (CA INDEX NAME)



L6 ANSWER 317 OF 319 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1946:37330 HCAPLUS
 DOCUMENT NUMBER: 40:37330
 ORIGINAL REFERENCE NO.: 40:7212h-i,7213a-b
 TITLE: Preparation of 4-mercpto- and 4-aminoquinazolines
 AUTHOR(S): Leonard, Nelson J.; Curtin, David Y.
 CORPORATE SOURCE: Univ. of Illinois, Urbana
 SOURCE: Journal of Organic Chemistry (1946), 11, 349-52
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB The preparation of 4-aminoquinazolines from 4-quinazolone (I) via the 4-mercptoquinazoline (II) and 4-methylmercptoquinazoline (III) is described. When 15 g. I is refluxed in 100 cc. xylene with 21.6 g. P2S5 for 2 h., 70 cc. 20% NaOH added, the mixture filtered, the xylene distilled off, and the filtered solution slightly acidified with AcOH, a yellow precipitate is

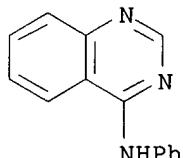
obtained. This is repptd. from 20% NaOH and refluxed with AcOH for 0.5 h. to give 59% II, m. 311-12° (324-5° (corrected)). Methylation of II with Me₂SO₄ and NaOH gives 85% III, m. 50-7°. When 1.5 g. crude III is heated with Et₂N(CH₂)₃NH₂ (IV) at 90-110° until MeSH is no longer evolved, the excess IV is removed with CS₂, and the reaction product added to a picric acid solution, 56% 4-(3-diethylaminopropylamino)quinazoline dipicrate (V), m. 195-9°, is obtained; free base, m. 58-63°. II and IV, heated for 20 min. at 90-110°, followed by addition of a picric acid solution, give 80% V, m. 197-200°. II and NH₂Bu refluxed for 2 h. give 70% 4-butylaminoquinazoline, m. 116-17° (picrate m. 189.5-90.5°). In a similar way, II and PhNH₂ heated for 4.5 h. give 14% 4-anilinoquinazoline (VI), m. 216-17° (picrate m. 230-1°). When II and PhNH₂ are heated for only 3 h. the yield of VI is 23%. II and morpholine, heated at 105-10° for 3.5 h., give 27% 4-morpholinoquinazoline, m. 93.5-4.5° (picrate m. 204-5°). When II is refluxed for 72 h. with NHEt₂, H is recovered unchanged.

IT 34923-95-0P, Quinazoline, 4-anilino-

RL: PREP (Preparation)
(preparation of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 318 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1946:8427 HCPLUS

DOCUMENT NUMBER: 40:8427

ORIGINAL REFERENCE NO.: 40:1523i,1524a-e

TITLE: Quinazolines. II. Properties of 4-substituted quinazolines

AUTHOR(S): Tomisek, Arthur J.; Christensen, Bert E.

CORPORATE SOURCE: Oregon State Coll., Corvallis

SOURCE: Journal of the American Chemical Society (1945), 67, 2112-15

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 40, 875.6. 4-Chloroquinazoline (I) is stable to aqueous bases, can be recrystd. from EtOH containing traces of NaOH, and reacts only slowly with alc. AgNO₃ in the absence of HNO₃. I (1 g.) and 5 cc. specially dried MeOH, shaken 15 min., give 91% of 4-methoxyquinazoline-HCl, m. 129° with conversion to 4-hydroxyquinazoline (II); if the MeOH solution of I is refluxed 24 h., there results 54% of II.HCl, which sublimes as II at about 150°; the II m. 212-15°. Finely powdered I, allowed to stand 1 day with concentrated NH₄OH, gives 70% of 4-aminoquinazoline, decomp. about 260°; di-HBr salt, prepared from the amine and EtOH-HBr, and mono-HBr salt, prepared by crystallization of the di-HBr salt from anhydrous Me₂CO-EtOH, m.

292° (decomposition); the amine is not acetylated by prolonged boiling in Ac₂O or AcCl or by the Schotten-Baumann method, but refluxed with Ac₂O in C₅H₅N for 18 h., it yields the Ac derivative, m. 172°. The

susceptibility to hydrolysis (1 g. of amine in 10 cc. dilute HCl at 85°) is in the order: 2,2'-dihydroxy-tert-butylamino, anilino, NH₂, and BuNH; conditions for 50% hydrolysis within 24 h. ranged from 2 to 3 equivs. of acid per mol of amine; the morpholino, piperidyl, and Et₂N derivs. hydrolyzed at from 10 to 50 times the above rate.

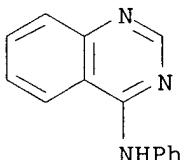
5-Nitro-4-hydroxy-2-methylquinazoline, reduced with Pd-C at 60° and 2-3 atmospheric H for 24 h., gives a quant. yield of the 5-NH₂ derivative, sublimes

and decomp. without melting; di-HBr salt; Ac derivative, sublimes about 180° but does not m. at 300°. Through the Sandmeyer reaction this yields 70% of 5-cyano-4-hydroxy-2-methylquinazoline, sublimes about 200° but does not m. at 300°; hydrolysis with concentrated HCl (20 h. at 160°) gives 4-hydroxy-2-methyl-5-quinazoliniccarboxylic acid-HCl; the free base sublimes at 235°. I does not react on fusion with AgCN or CuCN nor does it form a Mg complex in boiling Et₂O or Bu₂O. The 4-NH₂ derivative could not be diazotized at 0° or room temperature; it probably exists in the imino form. It is believed that I is activated by the H ion and its behavior supports the mechanism suggested by Banks (C.A. 38, 4952.5).

IT 34923-95-0, Quinazoline, 4-anilino-
(hydrolysis of)

RN 34923-95-0 HCPLUS

CN 4-Quinazolinamine, N-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 319 OF 319 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1931:52452 HCPLUS

DOCUMENT NUMBER: 25:52452

ORIGINAL REFERENCE NO.: 25:5898i,5899a-c

TITLE: Quinazolines. II. Interaction of 2,4-dichloroquinazoline in alcohol with salts and bases

AUTHOR(S): Lange, N. A.; Sheibley, F. E.

SOURCE: Journal of the American Chemical Society (1931), 53, 3867-75

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

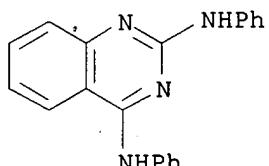
AB cf. C. A. 24, 5039. In part I it was shown that 2,4-dichloroquinazoline (I) reacted with Na alcohohlates to give the 2-chloro-4-alkoxy derivs. It is now shown that KCN, Na₂CO₃ or KCNO in MeOH or EtOH behaves in a similar manner. I and NaOAc on boiling give NaCl, AcOEt, chloroethoxyquinazoline, benzoyleneurea and a compound which appears to be 2(?) -chloro-4(?) -ketodihydroquinazoline, m. 211°, hydrolyzed by dilute acid to the urea; it could not be reduced to 4-ketodihydroquinazoline and did not react with EtONa to give the EtO derivative. The mechanism of its formation is discussed. Heating I and PhNH₂ in EtOH gives 2,4-dianilinoquinazoline, which seps. as the HCl salt, softens 304°, m. 317°; sulfate, m. 295°; acetate, m. 148°; nitrate, m. 223°; oxalate, m. 253°; picrate, deep yellow, m. 275°; the base crystallizes with EtOH of crystallization and loses 9.2% in weight at 40°; the base forms a hard, brittle, glassy mass, m. about 75°. Similarly p-H₂NC₆H₄CO₂H and I in EtOH give 2,4-dianilinoquinazoline-p,p' -

dicarboxylic acid-HCl, m. 347°; m,m'-isomer, m. 344°;
o,o'isomer, m. 271° (di-Me ester, m. 261°); the amphoteric
nature and the difficulties encountered in their purification resulted in
failure to isolate the free bases. 4-Chloroquinazoline and PhNH₂ at
100° give the 4-anilino derivative, m. 221-2°; HCl salt, m.
251°; picrate, yellow, m. 233°.

IT 27142-44-5, Quinazoline, 2,4-dianilino-
(and salts)

RN 27142-44-5 HCPLUS

CN 2,4-Quinazolinediamine, N,N'-diphenyl- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 09:43:33 ON 11 JAN 2007)

FILE 'REGISTRY' ENTERED AT 09:43:47 ON 11 JAN 2007

L1 STRUCTURE uploaded
L2 50 S L1 SAMPLE
L3 16567 S L1 FUL

FILE 'HCPLUS' ENTERED AT 09:44:24 ON 11 JAN 2007

L4 2367 S L3
L5 2358 S L4 NOT METHYLENEDIOXY
L6 319 S L5 NOT PY>1999

=> s 16 and (leukemia or lymphoma0

UNMATCHED LEFT PARENTHESIS 'AND (LEUKEMIA'

The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s 16 and (leukemia or lymphoma)

101593 LEUKEMIA
36254 LYMPHOMA

L7 7 L6 AND (LEUKEMIA OR LYMPHOMA)

=> d 17 1- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 7 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:735691 HCPLUS

DOCUMENT NUMBER: 132:202585

TITLE: In vivo toxicity and pharmacokinetic features of the
Janus kinase 3 inhibitor WHI-P131 [4-(4'hydroxyphenyl)-
amino-6,7-dimethoxyquinazoline]

AUTHOR(S): Uckun, Fatih M.; Ek, Onur; Liu, Xin-Ping; Chen,
Chun-Lin

CORPORATE SOURCE: Parker Hughes Cancer Center, Departments of Oncology,
Immunology, Drug Discovery Program, Hughes Institute,
St. Paul, MN, 55113, USA

SOURCE: Clinical Cancer Research (1999), 5(10), 2954-2962

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB 4-(4'Hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) is a potent and selective inhibitor of the Janus kinase 3, which triggers apoptosis in human acute lymphoblastic leukemia (ALL) cells. In this preclin. study, we evaluated the pharmacokinetics and toxicity of WHI-P131 in rats, mice, and cynomolgus monkeys. Following i.v. administration, the terminal elimination half-life of WHI-P131 was 73.2 min in rats, 103.4 min in mice, and 45.0 min in monkeys. The i.v. administered WHI-P131 showed a very wide tissue distribution in mice. Following i.p. administration, WHI-P131 was rapidly absorbed in both rats and mice, and the time to reach the maximum plasma concentration (tmax) was 24.8 min in rats and 10.0 min in mice.

Subsequently, WHI-P131 was eliminated with a terminal elimination half-life of 51.8 min in rats and 123.6 min in mice. The estimated i.p. bioavailability was 95% for rats, as well as for mice. WHI-P131 was quickly absorbed after oral administration in mice with a tmax of 5.8 min, but its oral bioavailability was relatively low (29.6%). The elimination half-life of WHI-P131 after oral administration was 297.6 min. WHI-P131 was not acutely toxic to mice at single i.p. bolus doses ranging from 0.5-250 mg/kg. Two cynomolgus monkeys treated with 20 mg/kg WHI-P131 and one cynomolgus monkey treated with 100 mg/kg WHI-P131 experienced no side effects. Plasma samples from WHI-P131-treated monkeys exhibited potent antileukemic activity against human ALL cells in vitro. To our knowledge, this is the first preclin. toxicity and pharmacokinetic study of a Janus kinase 3 inhibitor. Further development of WHI-P131 may provide the basis for new and effective treatment programs for relapsed ALL in clin. settings.

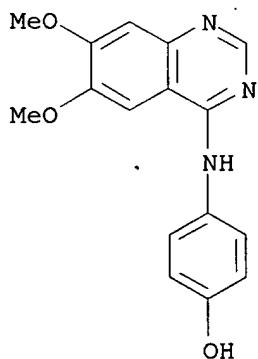
IT 202475-60-3, WHI-P131

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(in vivo toxicity and pharmacokinetic features of the Janus kinase 3 inhibitor WHI-P131)

RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



PROV 30
out

REFERENCE COUNT:

20

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:428003 HCAPLUS

DOCUMENT NUMBER: 131:295193
 TITLE: Structure-based design of specific inhibitors of janus kinase 3 as apoptosis-inducing antileukemic agents
 AUTHOR(S): Sudbeck, Elise A.; Liu, Xing-Ping; Narla, Rama Krishna; Mahajan, Sandeep; Ghosh, Sutapa; Mao, Chen; Uckun, Fatih M.
 CORPORATE SOURCE: Parker Hughes Cancer Center, Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Clinical Cancer Research (1999), 5(6), 1569-1582
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A novel homol. model of the kinase domain of Janus kinase (JAK) 3 was used for the structure-based design of dimethoxyquinazoline compds. with potent and specific inhibitory activity against JAK3. The active site of JAK3 in this homol. model measures roughly 8 Å + 11 Å + 20 Å, with a volume of .apprx.530 Å³ available for inhibitor binding. Modeling studies indicated that 4-(phenylamino)-6,7-dimethoxyquinazoline (WHI-258) (I) would likely fit into the catalytic site of JAK3 and that derivs. of I that contain an OH group at the 4' position of the Ph ring would more strongly bind to JAK3 because of added interactions with Asp-967, a key residue in the catalytic site of JAK3. These predictions were consistent with docking studies indicating that compds. containing a 4-OH group, WHI-P131 [4-((4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P154 [4-((3-bromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P97 [4-((3,5-dibromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], were likely to bind favorably to JAK3, with estimated Kis ranging from 0.6 to 2.3 μM. These compds. inhibited JAK3 in immune complex kinase assays in a dose-dependent fashion. In contrast, compds. lacking the 4-OH group, WHI-P79 [4-((3-bromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P111 [4-((3-bromo-4-methylphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P112 [4-((2,5-dibromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P132 [4-((2-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P258 [4-(phenylamino)-6,7-dimethoxyquinazoline], were predicted to bind less strongly, with estimated Kis ranging from 28 to 72 μM. These compds. did not show any significant JAK3 inhibition in kinase assays. Furthermore, the lead dimethoxyquinazoline compound, WHI-P131, which showed potent JAK3-inhibitory activity (IC₅₀ of 78 μM), did not inhibit JAK1 and JAK2, the ZAP/SYK family tyrosine kinase SYK, the TEC family tyrosine kinase BTK, the SRC family tyrosine kinase LYN, or the receptor family tyrosine kinase insulin receptor kinase, even at concns. as high as 350 μM. WHI-P131 induced apoptosis in JAK3-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma (M24-MET) or squamous carcinoma (SQ20B) cells. Leukemia cells were not killed by dimethoxyquinazoline compds. that were inactive against JAK3. WHI-P131 inhibited the clonogenic growth of JAK3-pos. leukemia cell lines DAUDI, RAMOS, LC1;19, NALM-6, MOLT-3, and HL-60 (but not JAK3-neg. BT-20 breast cancer, M24-MET melanoma, or SQ20B squamous carcinoma cell lines) in a concentration-dependent fashion. Potent and specific inhibitors of JAK3 such as

WHI-P131 may provide the basis for the design of new treatment strategies against acute lymphoblastic leukemia, the most common form of childhood cancer.

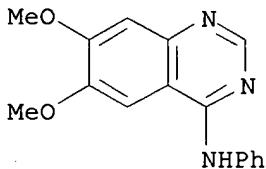
IT 21561-09-1 153436-54-5 202475-60-3, WHI-P131
 211555-04-3, WHI-P154 211555-05-4 211555-06-5
 211555-07-6 247080-98-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(structure-based design of specific inhibitors of janus kinase 3 as apoptosis-inducing antileukemic agents)

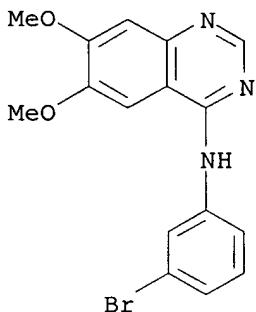
RN 21561-09-1 HCAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



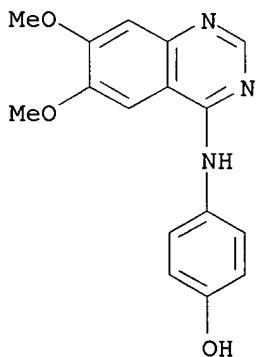
RN 153436-54-5 HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



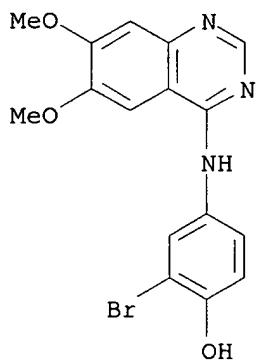
RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



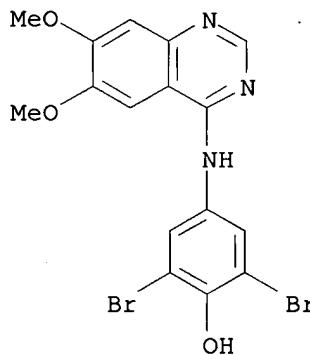
RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



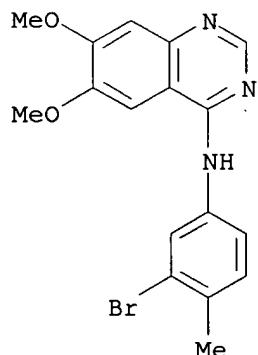
RN 211555-05-4 HCAPLUS

CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



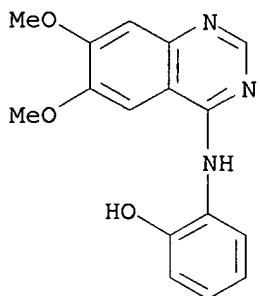
RN 211555-06-5 HCAPLUS

CN 4-Quinazolinamine, N- (3-bromo-4-methylphenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

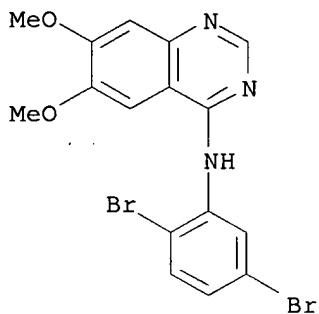


RN 211555-07-6 HCAPLUS

CN Phenol, 2-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 247080-98-4 HCAPLUS
 CN 4-Quinazolinamine, N-(2,5-dibromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:492839 HCAPLUS
 DOCUMENT NUMBER: 129:213579
 TITLE: Role of tyrosine kinases in induction of the c-jun proto-oncogene in irradiated B-lineage lymphoid cells
 AUTHOR(S): Goodman, Patricia A.; Niehoff, Lisa B.; Uckun, Fatih M.
 CORPORATE SOURCE: Department of Molecular Genetics, Wayne Hughes Institute, St. Paul, MN, 55113, USA
 SOURCE: Journal of Biological Chemistry (1998), 273(28), 17742-17748
 CODEN: JBCHA3; ISSN: 0021-9258
 PUBLISHER: American Society for Biochemistry and Molecular Biology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Exposure of B-lineage lymphoid cells to ionizing radiation induces an elevation of c-jun proto-oncogene mRNA levels. This signal is abrogated by protein-tyrosine kinase (PTK) inhibitors, indicating that activation of an as yet unidentified PTK is mandatory for radiation-induced c-jun expression. Here, we provide exptl. evidence that the cytoplasmic tyrosine kinases BTK, SYK, and LYN are not required for this signal. Lymphoma B-cells rendered deficient for LYN, SYK, or both by targeted gene disruption showed increased c-jun expression levels after radiation exposure, but the magnitude of the stimulation was lower than in wild-type cells. Thus, these PTKs may participate in the generation of an optimal signal. Notably, an inhibitor of JAK-3 (Janus family kinase-3)

abrogated radiation-induced c-jun activation, prompting the hypothesis that a chicken homolog of JAK-3 may play a key role in initiation of the radiation-induced c-jun signal in B-lineage lymphoid cells.

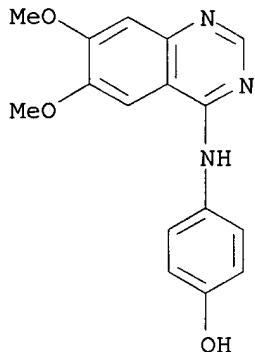
IT 202475-60-3P 211555-04-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOI (Biological study); PREP (Preparation)

(role of tyrosine kinases in induction of c-jun proto-oncogene in irradiated B-lineage lymphoid cells)

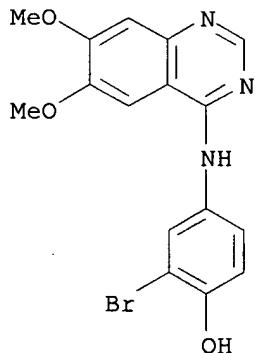
RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:401227 HCAPLUS

DOCUMENT NUMBER: 129:170172

TITLE: 4-(3'-Bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline: a novel quinazoline derivative with potent cytotoxic activity against human glioblastoma cells

AUTHOR(S): Narla, Rama Krishna; Liu, Xing-Ping; Myers, Dorothea E.; Uckun, Fatih M.

CORPORATE SOURCE: Department of Experimental Oncology, Hughes Institute,

SOURCE: St. Paul, MN, 55113, USA
 Clinical Cancer Research (1998), 4(6), 1405-1414
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

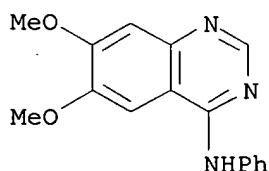
AB The novel quinazoline derivative 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) exhibited significant cytotoxicity against U373 and U87 human glioblastoma cell lines, causing apoptotic cell death at micromolar concns. The in vitro antiglioblastoma activity of WHI-P154 was amplified >200-fold and rendered selective by conjugation to recombinant human epidermal growth factor (EGF). The EGF-P154 conjugate was able to bind to and enter target glioblastoma cells within 10-30 min via receptor (R)-mediated endocytosis by inducing internalization of the EGF-R mols. In vitro treatment with EGF-P154 resulted in killing of glioblastoma cells at nanomolar concns. with an IC₅₀ of 813 ± 139 nM, whereas no cytotoxicity against EGF-R-neg. leukemia cells was observed, even at concns. as high as 100 µM. The in vivo administration of EGF-P154 resulted in delayed tumor progression and improved tumor-free survival in a severe combined immunodeficient mouse glioblastoma xenograft model. Whereas none of the control mice remained alive tumor-free beyond 33 days (median tumor-free survival, 19 days) and all control mice had tumors that rapidly progressed to reach an average size of >500 mm³ by 58 days, 40% of mice treated for 10 consecutive days with 1 mg/kg/day EGF-P154 remained alive and free of detectable tumors for more than 58 days with a median tumor-free survival of 40 days. The tumors developing in the remaining 60% of the mice never reached a size >50 mm³. Thus, targeting WHI-P154 to the EGF-R may be useful in the treatment of glioblastoma multiforme.

IT 21561-09-1P 153436-54-5P 202475-60-3P
 211555-04-3P 211555-05-4P 211555-06-5P
 211555-07-6P 211555-08-7P 211555-09-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glioblastoma inhibition by quinazoline derivative WHI-P154 targeting of EGF receptor)

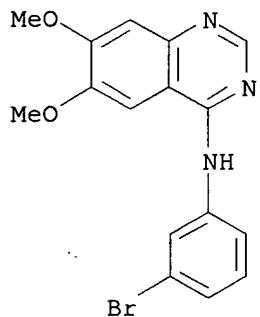
RN 21561-09-1 HCPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



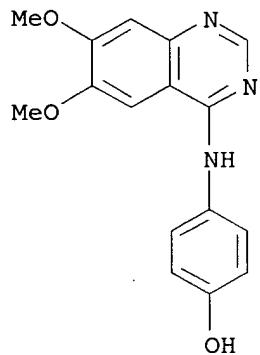
RN 153436-54-5 HCPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



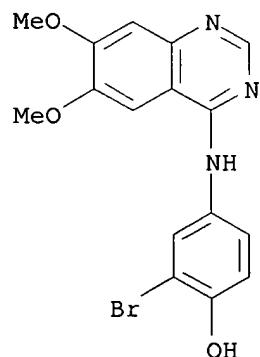
RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



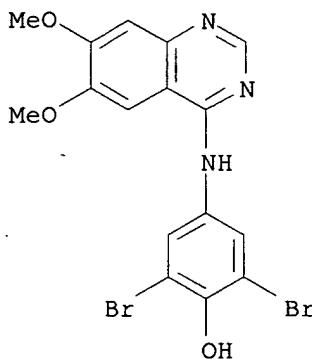
RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

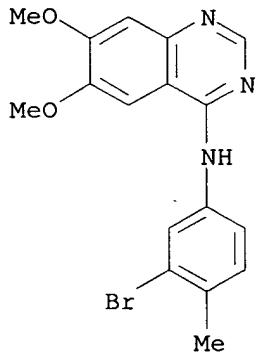


RN 211555-05-4 HCAPLUS

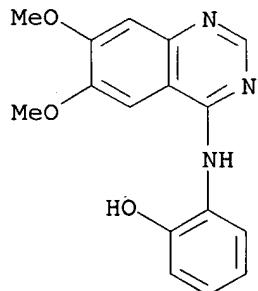
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



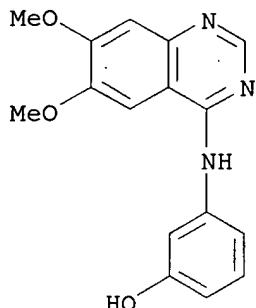
RN 211555-06-5 HCPLUS
CN 4-Quinazolinamine, N-(3-bromo-4-methylphenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



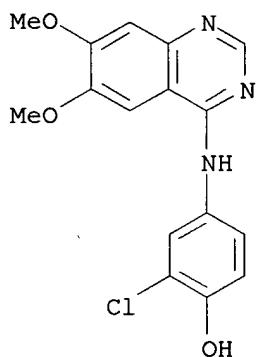
RN 211555-07-6 HCPLUS
CN Phenol, 2-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-08-7 HCPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-09-8 HCAPLUS
 CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

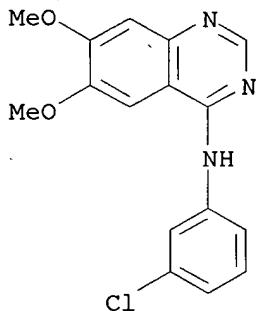


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

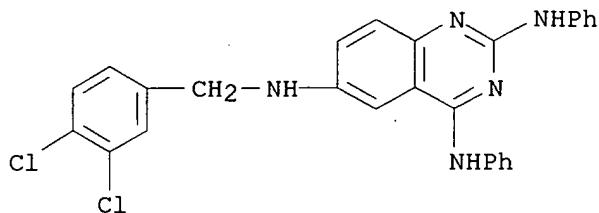
L7 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:116898 HCAPLUS
 DOCUMENT NUMBER: 124:249905
 TITLE: Inhibition of acute lymphoblastic leukemia by a Jak-2 inhibitor
 AUTHOR(S): Meydan, Naftaly; Grunberger, Tom; Dadi, Harjit;
 Shahar, Michal; Arpaia, Enrico; Lapidot, Zvi; Leeder,
 J. Steven; Freedman, Melvin; Cohen, Amos; et al.
 CORPORATE SOURCE: The Hospital for Sick Children, Univ. Toronto,
 Toronto, M5G 1X8, Can.
 SOURCE: Nature (London) (1996), 379(6566), 645-8
 CODEN: NATUAS; ISSN: 0028-0836
 PUBLISHER: Macmillan Magazines
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Acute lymphoblastic leukemia (ALL) is the most common cancer of childhood. Despite the progress achieved in its treatment, 20% of cases relapse and no longer respond to chemotherapy. The most common phenotype of all cells share surface antigens with very early precursors of B cells and are therefore believed to originate from this lineage. Characterization of the growth requirement of ALL cells indicated that they were dependent on various cytokines, suggesting paracrine and/or autocrine growth regulation. Because many cytokines induce tyrosine phosphorylation in lymphoid progenitor cells, and constitutive tyrosine

phosphorylation is commonly observed in B-lineage leukemias, attempts have been made to develop protein tyrosine kinase (PTK) blockers of leukemia cell growth. Here the authors show that leukemic cells from patients in relapse have constitutively activated Jak-2 PTK. Inhibition of Jak-2 activity by a specific tyrosine kinase blocker, AG-490, selectively blocks leukemic cell growth in vitro and in vivo by inducing programmed cell death, with no deleterious effect on normal hematopoiesis. None of the other tyrphostins tested had any activity against leukemic cells.

IT 153436-53-4, AG 1478
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibition of acute lymphoblastic leukemia by a Jak-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)
 RN 153436-53-4 HCPLUS
 CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L7 ANSWER 6 OF 7 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:89 HCPLUS
 DOCUMENT NUMBER: 82:89
 TITLE: Inhibition of mammalian dihydrofolate reductase by selected 2,4-diaminoquinazolines and related compounds
 AUTHOR(S): Richter, W. E., Jr.; McCormack, J. J.
 CORPORATE SOURCE: Coll. Med., Univ. Vermont, Burlington, VT, USA
 SOURCE: Journal of Medicinal Chemistry (1974), 17(9), 943-7
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Several of the 65 substituted diaminopyridopyrimidines, diaminopteridines, and diaminoquinazolines tested were active inhibitors of dihydrofolate reductase [9002-03-3] from rat liver and L1210 mouse leukemia cells. 2,4-Diamino-6-[(3,4-dichlorobenzyl)methylamino]quinazoline (I) [53274-32-1] was as active an inhibitor of the rat liver reductase as methotrexate [59-05-2]. Structure-activity relations were discussed.
 IT 38918-13-7
 RL: BIOL (Biological study)
 (dihydrofolate reductase inhibition by)
 RN 38918-13-7 HCPLUS
 CN 2,4,6-Quinazolinetriamine, N6-[(3,4-dichlorophenyl)methyl]-N2,N4-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1973:542776 HCAPLUS

DOCUMENT NUMBER: 79:142776

TITLE: Potential antitumor agents. 13. Bisquaternary salts

AUTHOR(S): Atwell, G. J.; Cain, B. F.

CORPORATE SOURCE: Cancer Chemother. Lab., Cornwall Geriatr. Hosp., Auckland, N. Z.

SOURCE: Journal of Medicinal Chemistry (1973), 16(6), 673-8
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 4-Anilinoquinolinium compounds bearing any of a number of quaternary N substituents on the phenyl ring were active in mice against L1210 leukemia. Activity was enhanced by the electron-donor substituents such as an amino group on the quinoline nucleus, as in 6-amino-1-ethyl-4-[p-[p-[(1-ethylpyridinium-4-yl)amino]phenylcarbamoyl]anilino]quinolinium dibromide (I) [42013-69-4], or by a 7-nitro group. I at 0.67 mg/kg/day i.p. for 5 days, given to mice inoculated i.p. with 105 L1210 cells 1 day previously, increased the life span by 40% and 2 out of 6 inoculated mice survived for 100 days when treated with 6.7 mg I/kg/day for 5 days. This survival indicated a lower toxicity of I (and of several related compds. tested) and of some bisquaternary antileukemics reported previously. I was prepared by condensation of 4-chloro-1-ethyl-6-nitroquinolinium [42013-70-7], prepared from 6-nitro-4-hydroxyquinoline [23432-42-0], with 1-ethyl-4-[4-(4-aminobenzamido)anilino]pyridinium [42013-72-9], followed by a reduction of the NO₂ group to NH₂.

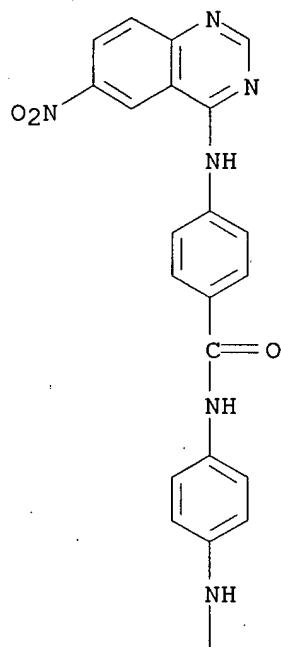
IT 50440-33-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)

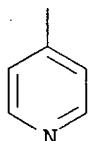
RN 50440-33-0 HCAPLUS

CN Benzamide, 4-[(6-nitro-4-quinazolinyl)amino]-N-[4-(4-pyridinylamino)phenyl]- (9CI) (CA INDEX NAME)

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=> d_his

(FILE 'HOME' ENTERED AT 09:43:33 ON 11 JAN 2007)

FILE 'REGISTRY' ENTERED AT 09:43:47 ON 11 JAN 2007

L1 STRUCTURE UPLOADED
L2 50 S L1 SAMPLE
L3 16567 S L1 FUL

FILE 'HCAPLUS' ENTERED AT 09:44:24 ON 11 JAN 2007

L4 2367 S L3
L5 2358 S L4 NOT METHYLENEDIOXY
L6 319 S L5 NOT PY>1999
L7 7 S L6 AND (LEUKEMIA OR LYMPHOMA)

=> log y